02-05-2010

10/598,789A Yong Chu ~~07-08-2008~~

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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JAN 02	STN pricing information for 2008 now available
NEWS 3	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 5	JAN 28	MARPAT searching enhanced
NEWS 6	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS 9	FEB 08	STN Express, Version 8.3, now available
NEWS 10	FEB 20	PCI now available as a replacement to DPCI
NEWS 11	FEB 25	IFIREF reloaded with enhancements
NEWS 12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS 14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS 15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS 16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS 17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS 18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS 20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS 22	APR 28	IMSRESEARCH reloaded with enhancements
NEWS 23	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS 24	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS 25	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS 26	JUN 06	KOREAPAT updated with 41,000 documents
NEWS 27	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS 28	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS 29	JUN 25	CA/CAplus and USPAT databases updated with IPC reclassification data
NEWS 30	JUN 30	AEROSPACE enhanced with more than 1 million U.S.

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                  patent records
 NEWS 31  JUN 30  EMBASE, EMBAL, and LEMBASE updated with additional
                  options to display authors and affiliated
                  organizations
 NEWS 32  JUN 30  STN on the Web enhanced with new STN AnaVist
                  Assistant and BLAST plug-in
 NEWS 33  JUN 30  STN AnaVist enhanced with database content from EPFULL

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 21:14:57 ON 08 JUL 2008

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 21:15:19 ON 08 JUL 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    7 JUL 2008  HIGHEST RN 1032964-85-4
DICTIONARY FILE UPDATES:   7 JUL 2008  HIGHEST RN 1032964-85-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Documents and Settings\ychu\Desktop\Case\10598789\10598789A.str
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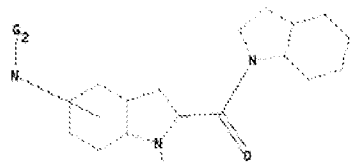
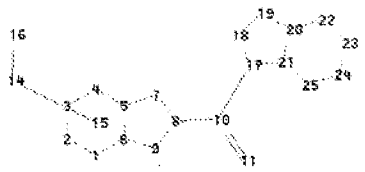




chain nodes :
10 11 13 14 16
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 22 23 24 25
chain bonds :
8-10 9-13 10-11 10-17 14-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-18 17-21 18-19 19-20 20-21
20-22 21-25 22-23 23-24 24-25
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-13 10-11 10-17 14-16 17-18
17-21 18-19 19-20 20-21 20-22 21-25 22-23 23-24 24-25
exact bonds :
8-10

G2:H,CH,t-Bu

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom
23:Atom 24:Atom 25:Atom

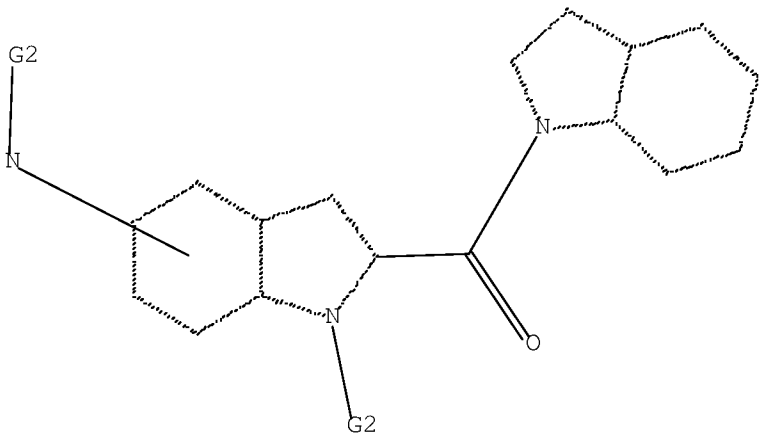
L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR

full scope

R1

Group II with claim 2



G1
G2 H,CH,t-Bu

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 21:16:01 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 511 TO ITERATE

100.0% PROCESSED 511 ITERATIONS 22 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8864 TO 11576
PROJECTED ANSWERS: 159 TO 721

L2 22 SEA SSS SAM L1

=> d dscan
'DSCAN' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
fields or predefined formats. The predefined substance formats
are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

EPROP - Table of experimental properties
PPROP - Table of predicted properties

PROP   - EPROP, ETAG, PPROP and SPEC

Any CA File format may be combined with any substance format to
obtain CA references citing the substance. The substance formats
must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

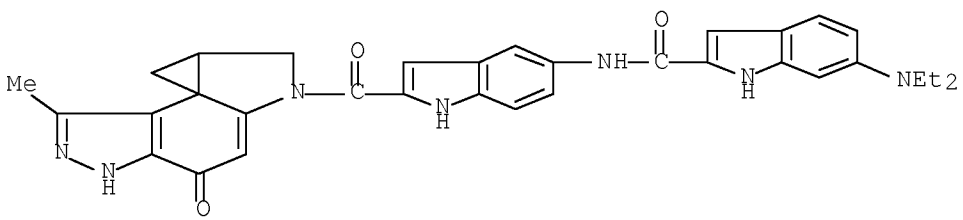
The ALL format gives FIDE BIB ABS IND RE, plus sequence data when
it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented,
with text labels.

For additional information, please consult the following help
messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> d scan

L2   22 ANSWERS   REGISTRY COPYRIGHT 2008 ACS on STN
IN   1H-Indole-2-carboxamide, 6-(diethylamino)-N-[2-[(4,5,8,8a-tetrahydro-7-
     methyl-4-oxocyclopropa[3,4]pyrrolo[3,2-e]indazol-2(1H)-yl)carbonyl]-1H-
     indol-5-yl]-
MF   C33 H31 N7 O3
CI   COM

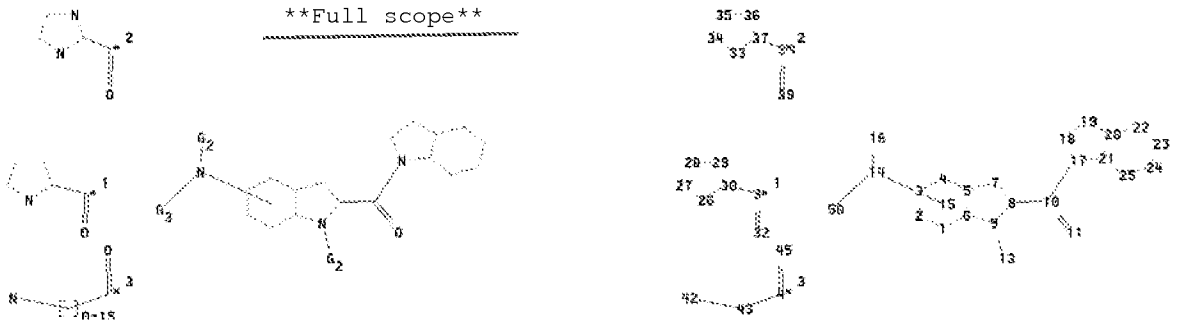


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=>
Uploading C:\Documents and Settings\ychu\Desktop\Case\10598789\10598789B.str

Full scope



chain nodes :
10 11 13 14 16 31 32 38 39 42 43 44 45 50
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 22 23 24 25 26 27 28 29 30
33 34 35 36 37
chain bonds :
8-10 9-13 10-11 10-17 14-16 14-50 30-31 31-32 37-38 38-39 42-43 43-44
44-45
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-18 17-21 18-19 19-20 20-21
20-22 21-25 22-23 23-24 24-25 26-27 26-30 27-28 28-29 29-30 33-34 33-37
34-35 35-36
36-37
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-13 10-11 10-17 14-16 14-50
17-18 17-21 18-19 19-20 20-21 20-22 21-25 22-23 23-24 24-25 26-27 26-30
27-28 28-29
29-30 31-32 33-34 33-37 34-35 35-36 36-37 38-39 42-43 44-45
exact bonds :
8-10 30-31 37-38 43-44

G2:H,CH,t-Bu

G3:[*1],[*2],[*3]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom
23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS
32:CLASS 33:Atom
34:Atom 35:Atom 36:Atom 37:Atom 38:CLASS 39:CLASS 42:CLASS 43:CLASS
44:CLASS 45:CLASS
50:CLASS

L3 STRUCTURE UPLOADED

=> d
L3 HAS NO ANSWERS
L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l3
SAMPLE SEARCH INITIATED 21:24:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 354 TO ITERATE

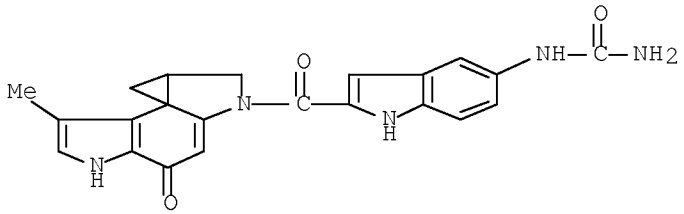
100.0% PROCESSED 354 ITERATIONS 13 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5952 TO 8208
PROJECTED ANSWERS: 44 TO 476

L4 13 SEA SSS SAM L3

=> d scan

L4 13 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Cyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, 2-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,8,8a-tetrahydro-7-methyl- (9CI)
MF C22 H19 N5 O3



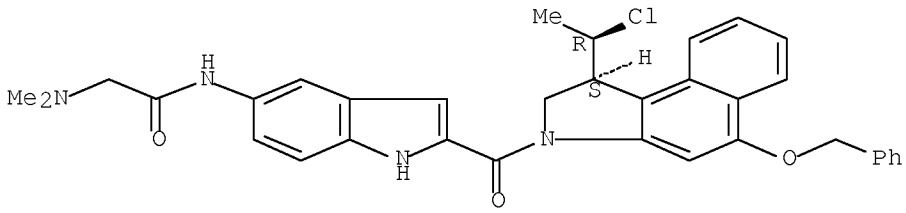
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L4 13 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Acetamide, N-[2-[[(1S)-1-[(1R)-1-chloroethyl]-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-2-

(dimethylamino)-
MF C34 H33 Cl N4 O3

Absolute stereochemistry. Rotation (+).

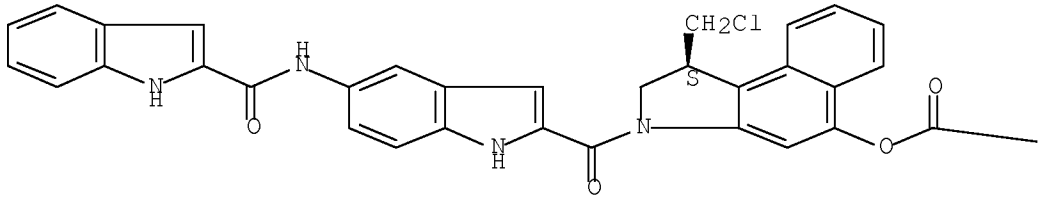


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

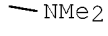
L4 13 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Carbamic acid, dimethyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI)
MF C34 H28 Cl N5 O4

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> s l13 full
L5 11 L13

=> s l3 full
FULL SEARCH INITIATED 21:25:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 7282 TO ITERATE

100.0% PROCESSED 7282 ITERATIONS 343 ANSWERS
SEARCH TIME: 00.00.01

L6 343 SEA SSS FUL L3

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 191.33 191.54

FILE 'CAPLUS' ENTERED AT 21:26:04 ON 08 JUL 2008
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FILE COVERS 1907 - 8 Jul 2008 VOL 149 ISS 2
FILE LAST UPDATED: 7 Jul 2008 (20080707/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

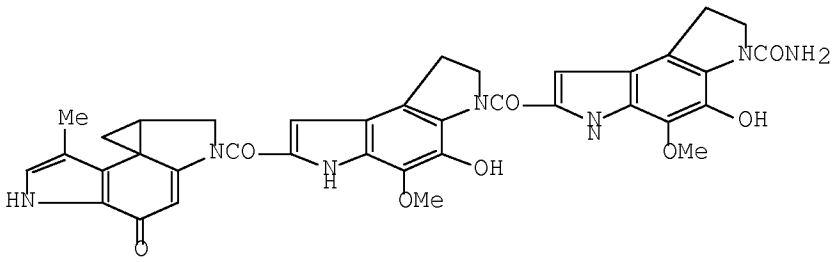
http://www.cas.org/legal/infopolicy.html

=> s l6
L7 183 L6 **Too many references**

=> d ibib abs hitstr 175-183

L7 ANSWER 175 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:124054 CAPLUS Full-text
DOCUMENT NUMBER: 108:124054
ORIGINAL REFERENCE NO.: 108:20145a,20148a
TITLE: Mutagenicity of the antitumor antibiotic CC-1065 and its analogs in mammalian (V79) cells and bacteria
AUTHOR(S): Harbach, Philip R.; Zimmer, David M.; Mazurek, John H.; Bhuyan, Bijoy K.
CORPORATE SOURCE: Dep. Pathol. Toxicol. Res., Upjohn Co., Kalamazoo, MI,

49001, USA
SOURCE: Cancer Research (1988), 48(1), 32-6
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



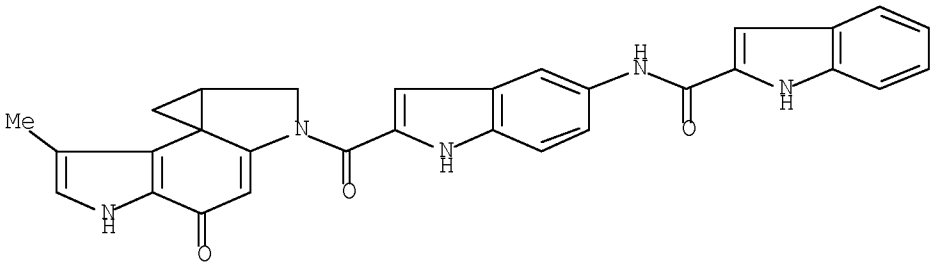
I

AB The mutagenicity for V79 cells (6-thioguanine resistance) and Salmonella (histidine auxotrophy or azaguanine resistance) of selected analogs of CC-1065 (I) was compared to DNA-binding activity and the structure-activity relationship was detd. CC-1065, U-62,736, U-66,866, U-66,694, U-67,786, and U-68,415 all have an A segment with an intact cyclopropyl group and different B segments. The cyclopropyl group is absent from U-66,226 and U-63,360. Elimination of the cyclopropyl ring diminished the cytotoxic and mutagenic potency of the compds. such that U-63,360 was nearly 3 orders of magnitude less potent than CC-1065 in V79 cells. For the compds. with an intact cyclopropyl group, the order of cytotoxic and mutagenic potency (molar basis) in V79 cells generally correlated with binding to calf thymus DNA, and increased with the length of the B segment. Thus, the order of cytotoxicity was CC-1065 > U-68,415 > U-66,694 > U-66,866 > U-62,736. U-67,786 cell outside this pattern since it was more cytotoxic and mutagenic than U-66,694, although it was of a similar size and had similar DNA-binding activity. These results show that an electrophilic C afforded by an intact cyclopropyl group of this type is necessary but not sufficient to account for the high cytotoxic and mutagenic potency of CC-1065 and U-68,415. The size and characteristics of the B segment also affect the potency. At an equitoxic (10 or 50% LD) dose, an inverse relationship exists between cytotoxic and mutagenic potency such that at the 50% LD, the least cytotoxic compd. (U-62,736) was more mutagenic than the most cytotoxic compd. (CC-1065). Apparently, the more cytotoxic analogs are less mutagenic (at an equitoxic dose) because they may have greater structure-directed binding to less mutable DNA sites in the minor groove.

IT 104713-40-8
RL: BIOL (Biological study)
(cytotoxic and mutagenic activities of, DNA binding in, structure in relation to)

RN 104713-40-8 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



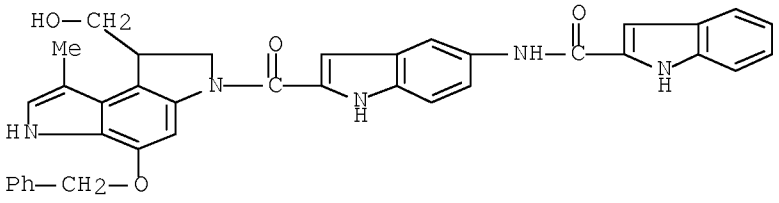
L7 ANSWER 176 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:94431 CAPLUS Full-text
DOCUMENT NUMBER: 108:94431
ORIGINAL REFERENCE NO.: 108:15531a,15534a
TITLE: Stereoelectronic factors influencing the biological activity and DNA interaction of synthetic antitumor agents modeled on CC-1065
AUTHOR(S): Warpehoski, M. A.; Gebhard, I.; Kelly, R. C.; Krueger, W. C.; Li, L. H.; McGovren, J. P.; Prairie, M. D.; Wicnienski, N.; Wierenga, W.
CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of Medicinal Chemistry (1988), 31(3), 590-603
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:94431
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

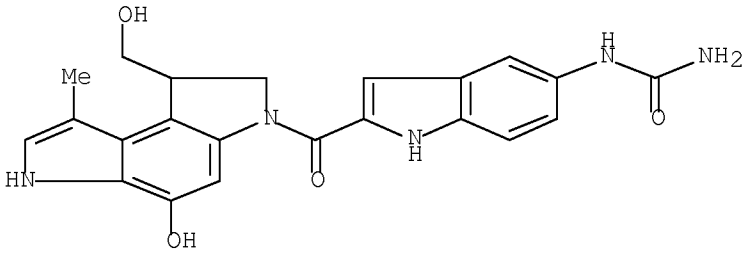
AB The synthesis, physicochem. properties, and biol. activities of 21 novel spiro cyclopropyl compds., e.g. I [R = H, SO2Ph, CO2CMe3, COMe, substituted (indol-2-yl)carbonyl], prepd. by intramol. cyclopropanation of pyrroloindoles II (R1 = PhCH2, R2 = SO2CF3; R1 = R2 = H), are described. Many I are more effective than the antitumor antibiotic CC-1065 (III) against murine tumors. In particular, IV exhibits high activity and potency. Structure-activity anal. supports a mol. mechanism of biol. action involving hydrophobic interaction of the drug with DNA and acid-catalyzed alkylation of DNA.

IT 101134-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and mesylation of)

RN 101134-50-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



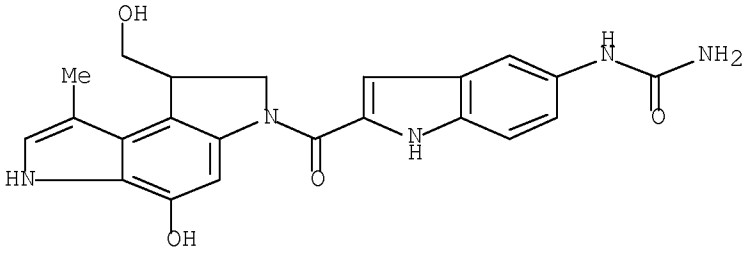
IT 112090-00-3P 112090-01-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 112090-00-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-5-hydroxy-8-methyl- (9CI) (CA INDEX NAME)



RN 112090-01-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-5-hydroxy-8-methyl-, monomethyl ether (9CI) (CA INDEX NAME)

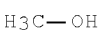
CM 1

CRN 112090-00-3
CMF C22 H21 N5 O4



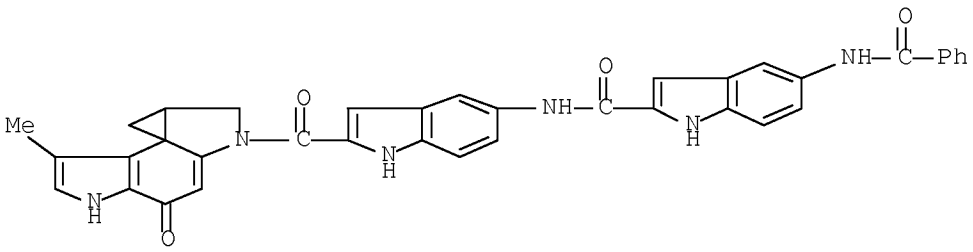
CM 2

CRN 67-56-1
CMF C H4 O

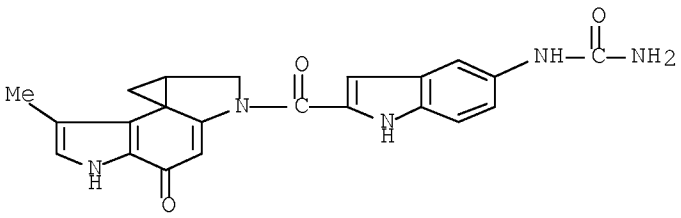


IT 101134-80-9P 101151-46-6P 101151-47-7P
104713-40-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., antitumor activity, induced CD, and kinetics of ring cleavage of)

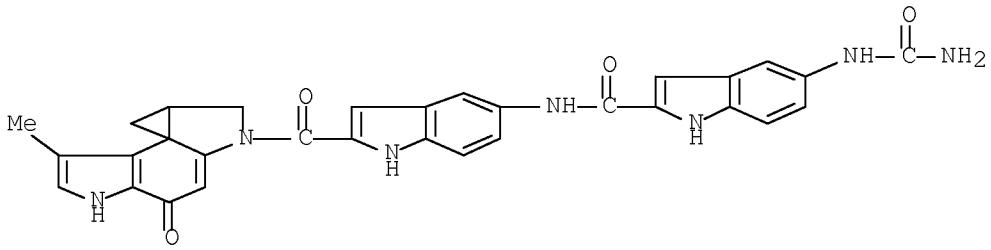
RN 101134-80-9 CAPLUS
CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



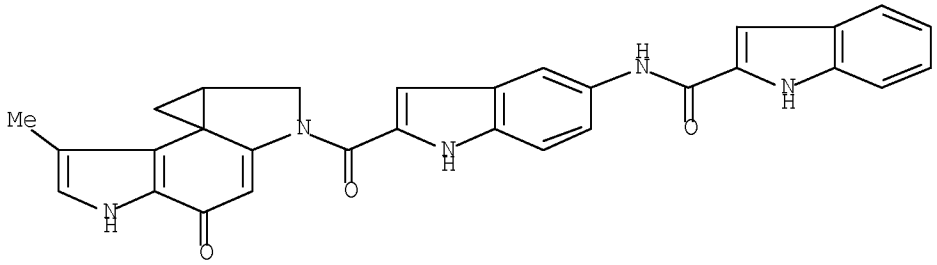
RN 101151-46-6 CAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, 2-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,8,8a-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 101151-47-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

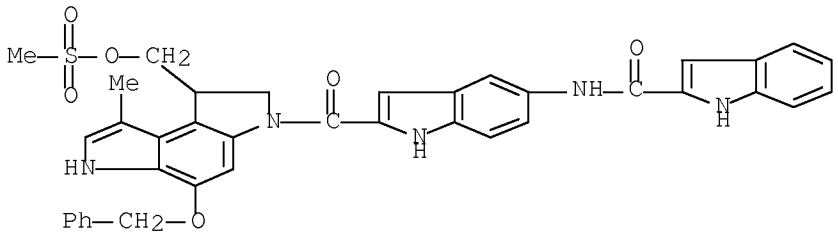


RN 104713-40-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

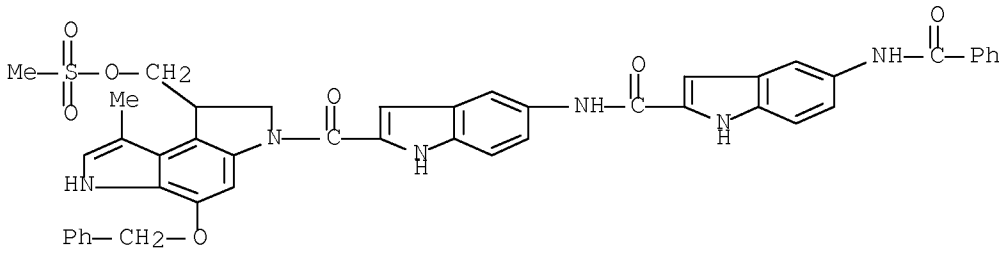


IT 101134-61-6P 101134-62-7P 101134-63-8P
101134-65-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., debenzylation, and intramol. cyclopropanation of)

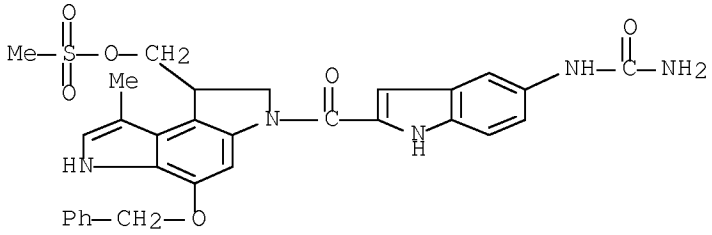
RN 101134-61-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



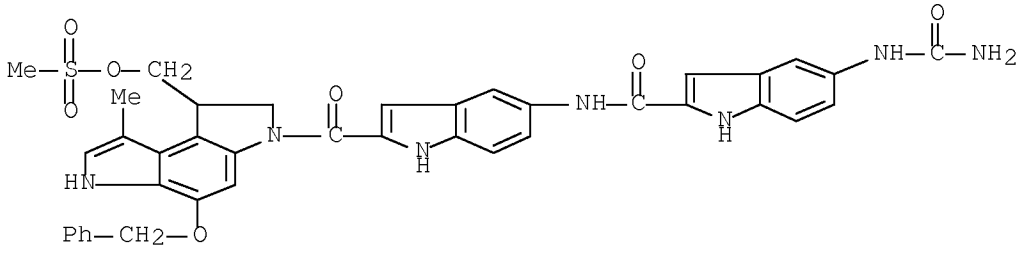
RN 101134-62-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



RN 101134-63-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



RN 101134-65-0 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L7 ANSWER 177 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:87686 CAPLUS Full-text
DOCUMENT NUMBER: 108:87686
ORIGINAL REFERENCE NO.: 108:14287a,14290a
TITLE: Effects of U-71,184 and several other CC-1065 analogs on cell survival and cell cycle of Chinese hamster ovary cells

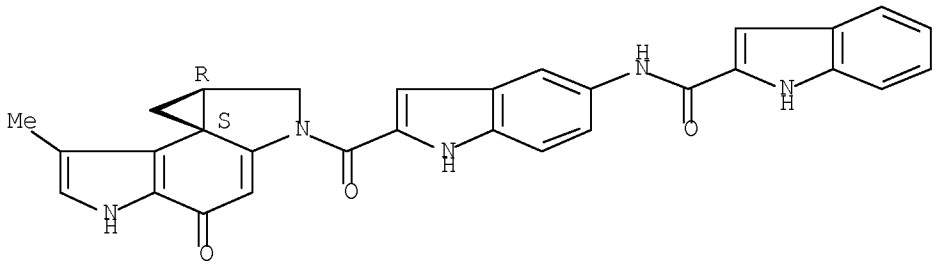
AUTHOR(S): Adams, Earl G.; Badiner, Gloria J.; Bhuyan, Bijoy K.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Cancer Research (1988), 48(1), 109-16
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of several analogs of CC-1065 on inhibition of CHO cell survival, cell progression, and their phase-specific toxicity are reported. CC-1065, U-66,664, U-66,819, U-66,694, and U-71,184 all have a left hand segment with an intact cyclopropyl group but have different tail segments. Lethality of these compds. after 2 h drug exposure was in the following order (50% lethal concn. in nM in parentheses): CC-1065 (0.06) > U-71,184 (1.3) > U-66,694 (3.2) > U-68,819 (171) > U-66,664 (>1200). In general, these compds. did not inhibit progression from G1 to S but slowed progression through S and blocked cells in G2-M. The phase-specific toxicity of U-71,184 and U-66,694 was different from that of CC-1065. CC-1065 was most cytotoxic to cells in M and early G1 and toxicity decreased as cells entered late G1 and S. In contrast, U-66,694 and U-71,184 were most toxic to cells in late G1. The biochem. and cellular effects of U-71,184 were then studied in detail since it was the most active among these analogs. After a 2-h exposure to 3 ng/mL U-71,184, 90% cell kill or growth inhibition was obsd., whereas 100 ng/mL was needed for similar inhibition of DNA and RNA synthesis. This discrepancy between the doses suggested that inhibition of nucleic acid synthesis may not be causally related to lethality. Further studies showed that when drug was removed after 2 h exposure, DNA synthesis continued to be inhibited, whereas RNA and protein synthesis reached levels higher than the control. Therefore, it is likely that at cytotoxic doses the low level of inhibition of DNA synthesis combined with the stimulation of RNA and protein synthesis leads to unbalanced growth and cell death.

IT 104713-39-5, U-71185
RL: PRP (Properties)
(cytotoxicity of, cell cycle in relation to)

RN 104713-39-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bS,8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 178 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:597901 CAPLUS Full-text
DOCUMENT NUMBER: 107:197901
ORIGINAL REFERENCE NO.: 107:31735a,31738a
TITLE: Coupling of cyclopropapyrroloindole (CPI) derivatives. The preparation of CC-1065, ent-CC-1065, and analogs

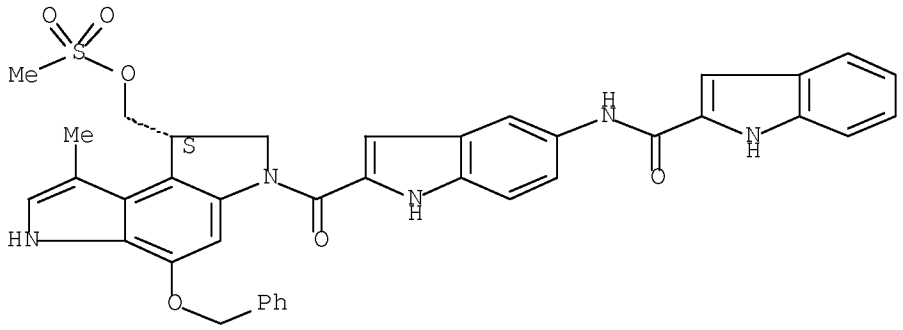
AUTHOR(S): Kelly, Robert C.; Gebhard, Ilse; Wicnienski, Nancy; Aristoff, Paul A.; Johnson, Paul D.; Martin, David G.
CORPORATE SOURCE: Cancer and Viral Dis. Res., Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of the American Chemical Society (1987), 109(22), 6837-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:197901
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB CC-1065 (I, R = R1) and its analogs I (R = pentyl, 2-indolyl, R2, X = NH, O) were prepd. from the pyrroloindole II (R3 = OH, R4 = H, R5 = CH2Ph) via II (R3 = Cl, R4 = CO2CMe3, R5 = H), II (R3 = Cl, R4 = R5 = H), and II (R3 = Cl, R4 = COR, R5 = H). Ent-CC-1065 was similarly prepd. and had an ED50 against leukemia L1210 of 4.5 .times. 10-12 g/mL.

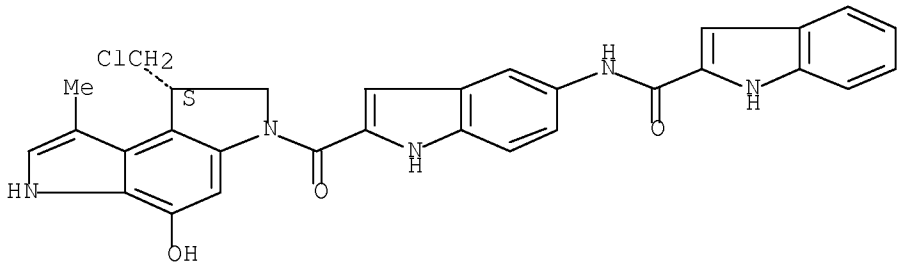
IT 108833-15-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and chlorination of)
RN 108833-15-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



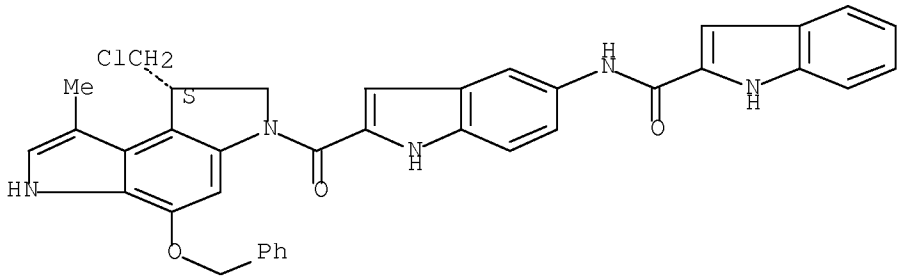
IT 110314-46-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclopropanation of)
RN 110314-46-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



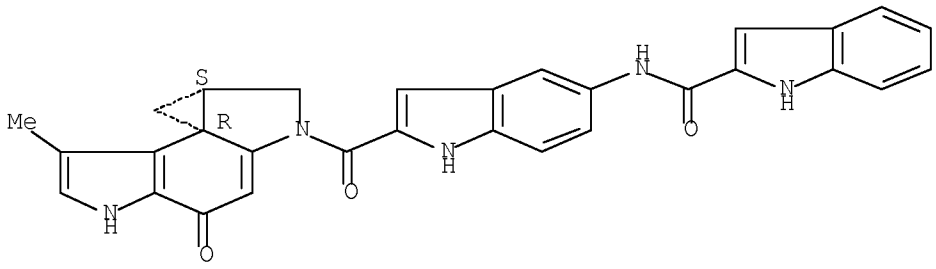
IT 110314-44-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenolysis of)
RN 110314-44-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

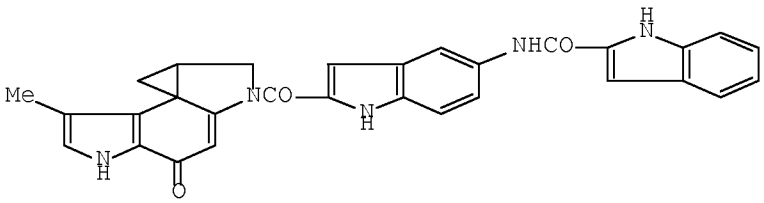


IT 101222-80-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 101222-80-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 179 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:423139 CAPLUS Full-text
DOCUMENT NUMBER: 107:23139
ORIGINAL REFERENCE NO.: 107:3903a,3906a
TITLE: Total synthesis of U-71184, a potent new antitumor agent modeled on CC-1065
AUTHOR(S): Warpehoski, M. A.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Tetrahedron Letters (1986), 27(35), 4103-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:23139
GI



I

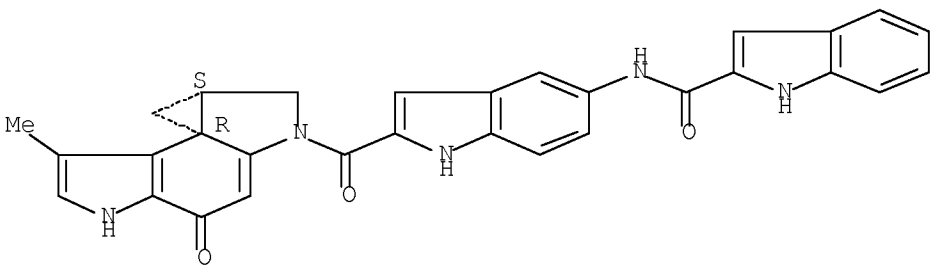
AB U-71184 (I), a highly potent analog of novel antitumor antibiotic CC-1065, involves the unmasking of a p-hydroxyphenethyl mesylate, which undergoes facile intramol. elimination to afford the reactive cyclopropylspirocyclohexadienone. Its enantiomer, U-71185, was also prepd. I had antitumor activity comparable to that of CC-1065 without the delayed toxicity, but U-71185 was inactive.

IT 101222-80-4P, U-71184 104713-39-5P, U-71185
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antitumor activity of)

RN 101222-80-4 CAPLUS

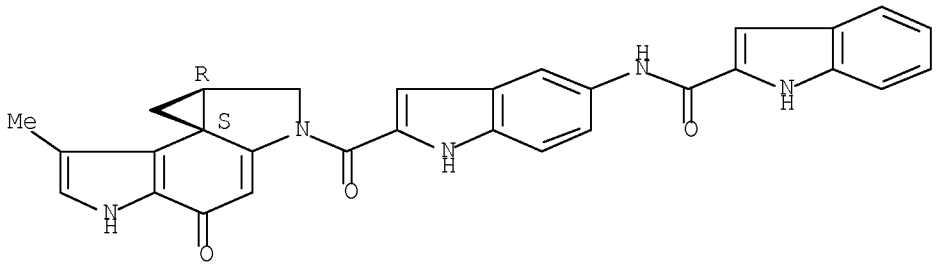
CN 1H-Indole-2-carboxamide, N-[2-[[(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



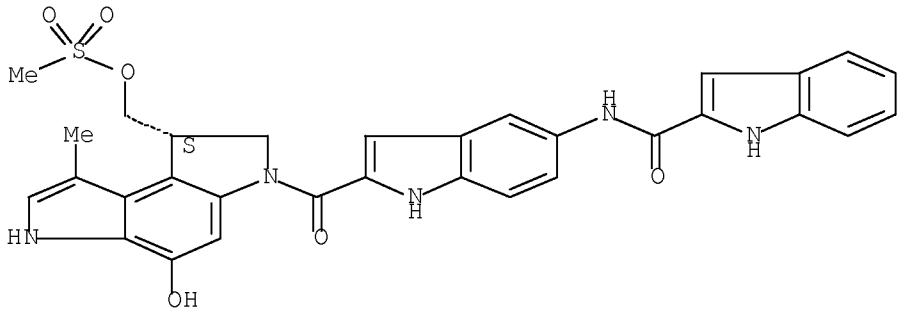
RN 104713-39-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bS,8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



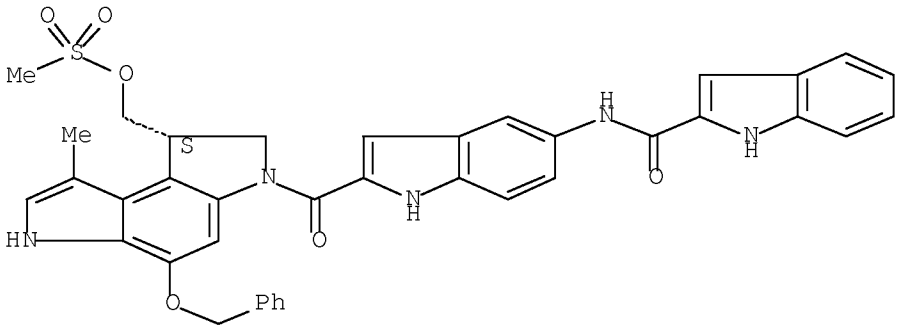
IT 108833-16-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclopropanation of)
RN 108833-16-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



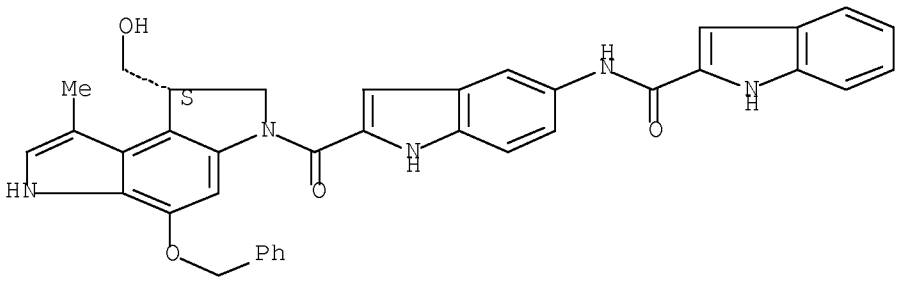
IT 108833-15-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzylation of)
RN 108833-15-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

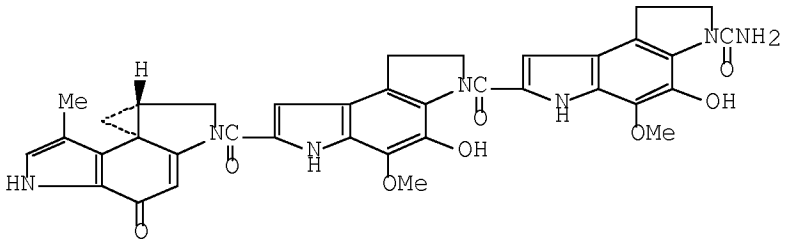


IT 108859-64-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and mesylation of)
RN 108859-64-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 180 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:12465 CAPLUS Full-text
DOCUMENT NUMBER: 106:12465
ORIGINAL REFERENCE NO.: 106:2037a,2040a
TITLE: L1210 cell growth inhibition, DNA synthesis inhibition, and DNA binding properties of CC-1065 analogs
AUTHOR(S): Krueger, W. C.; Prairie, M. D.; Wallace, T. L.; Moscowitz, A.; Li, L. H.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, USA
SOURCE: Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14th (1985), Volume Anticancer Sect. 1, 572-3. Editor(s): Ishigami, Joji. Univ. Tokyo Press: Tokyo, Japan.
CODEN: 55GNAX
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
GI



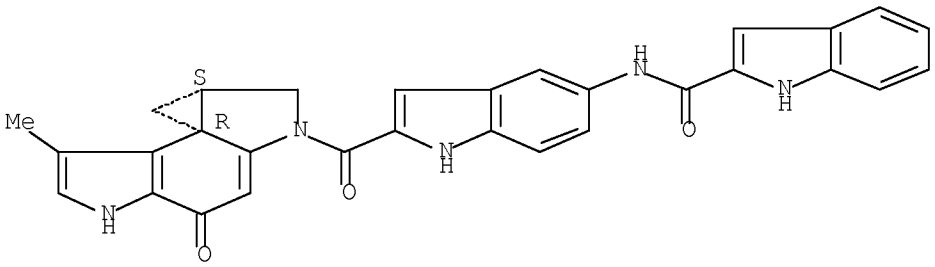
I

AB The biol. and biochem. activities of some analogs of the highly potent but toxic antitumor antibiotic ML-1065 (I) [69866-21-3] are compared to their DNA binding properties. In general, the binding affinity correlates with potency in the P388 activity and the degree of inhibition of L1210 cell growth and macromol. synthesis.

IT 101222-80-4 104713-39-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor activity of and DNA binding by and DNA formation response to)

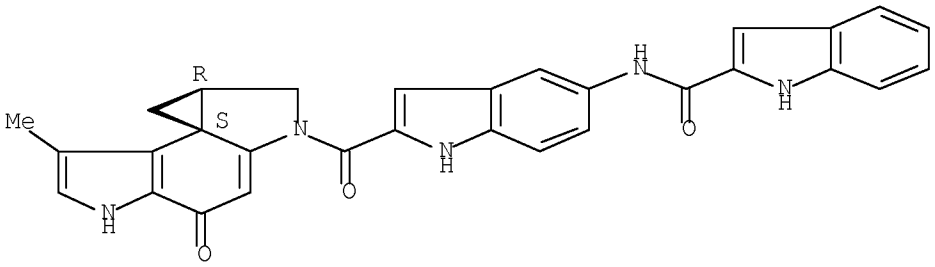
RN 101222-80-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

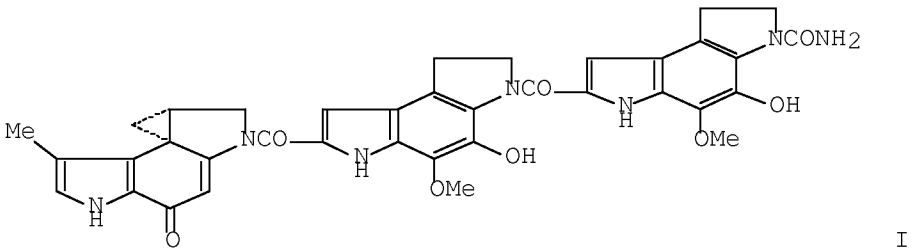


RN 104713-39-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bS,8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

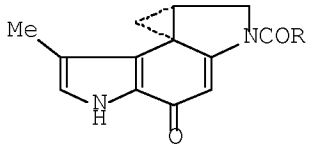
Absolute stereochemistry. Rotation (-).



L7 ANSWER 181 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:291 CAPLUS Full-text
DOCUMENT NUMBER: 106:291
ORIGINAL REFERENCE NO.: 106:55a
TITLE: N-2-substituted tetrahydro-4-oxocyclopropa[c]pyrrolo[3,2-e]indoles: novel anticancer agents modeled on CC-1065
AUTHOR(S): Warpehoski, M. A.; Kelly, R. C.; McGovren, J. P.; Wierenga, W.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, USA
SOURCE: Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14th (1985), Volume Anticancer Sect. 1, 570-1. Editor(s): Ishigami, Joji. Univ. Tokyo Press: Tokyo, Japan.
CODEN: 55GNAX
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



I



II

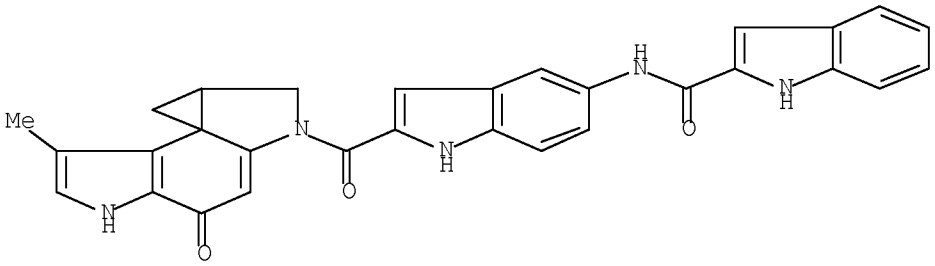
AB The antitumor activity of ML-1065 (I) [69866-21-3] and its analogs II (R = Me, 2-quinolinyl, 2-pyrrolyl, 2-indolyl, etc.) is described. Analogs with acyl, aroyl, and heteroaroyl substituents on N-2 of II had generated 2 highly active subgroups differentiated by DNA binding. Several DNA-binding analogs

exhibited similar potency to I but significantly improved antitumor activity (murine and human) with an absence of delayed lethality.

IT 104713-40-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of)

RN 104713-40-8 CAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



L7 ANSWER 182 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:564557 CAPLUS Full-text

DOCUMENT NUMBER: 105:164557

ORIGINAL REFERENCE NO.: 105:26357a,26360a

TITLE: Antitumor activity and biochemistry of novel analogs of the antibiotic, CC-1065

AUTHOR(S): Wierenga, W.; Bhuyan, B. K.; Kelly, R. C.; Krueger, W. C.; Li, L. H.; McGovren, J. P.; Swenson, D. H.; Warpehoski, M. A.

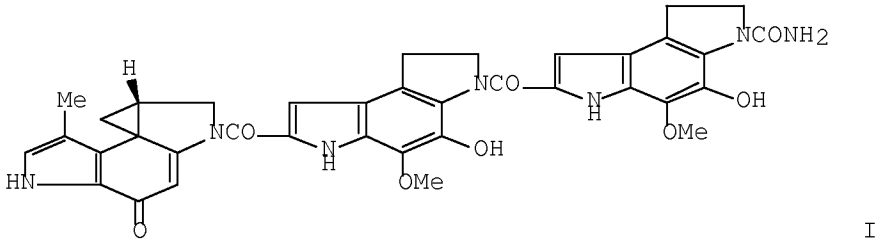
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA

SOURCE: Advances in Enzyme Regulation (1986), 25, 141-55
CODEN: AEZRA2; ISSN: 0065-2571

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

GI



I

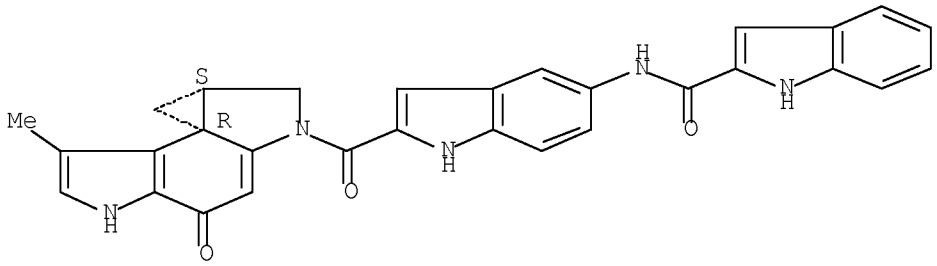
AB A discussion on the in vitro and in vivo antitumor activities of ML-1065 (I) [69866-21-3] and its analogs is presented. The effects of these compds. on

macromol. (DNA, protein, and RNA) biosynthesis and cell cycle are discussed. A review of previous work is included.

IT 101222-80-4 104713-39-5 104713-40-8
RL: PRP (Properties)
(antitumor activity and biochem. effects of, in humans and lab. animals)

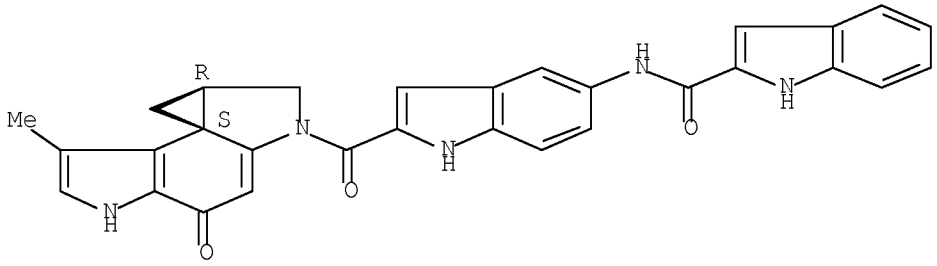
RN 101222-80-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

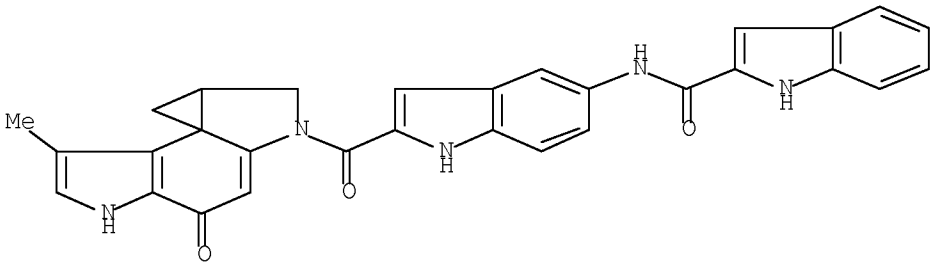


RN 104713-39-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bS,8aR)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 104713-40-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



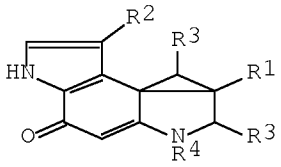
L7 ANSWER 183 OF 183 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:148641 CAPLUS Full-text
DOCUMENT NUMBER: 104:148641
ORIGINAL REFERENCE NO.: 104:23517a,23520a
TITLE: Analogs of antibiotic CC-1065
INVENTOR(S): Kelly, Robert Charles; Warpehoski, Martha Ann; Wierenga, Wendell
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: Eur. Pat. Appl., 96 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 154445	A1	19850911	EP 1985-301125	19850220
EP 154445	B1	19890531		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4912227	A	19900327	US 1986-894314	19860807
JP 08225573	A	19960903	JP 1995-331640	19951220

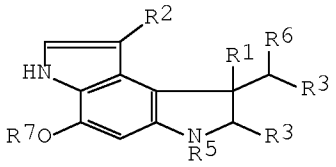
PRIORITY APPLN. INFO.:

US 1984-581836	A	19840221
US 1985-694363	A	19850124
CA 1985-473917	A	19850208
ZA 1985-1093	A	19850213
EP 1985-301125	A	19850220
JP 1985-31662	A	19850221

GI



I



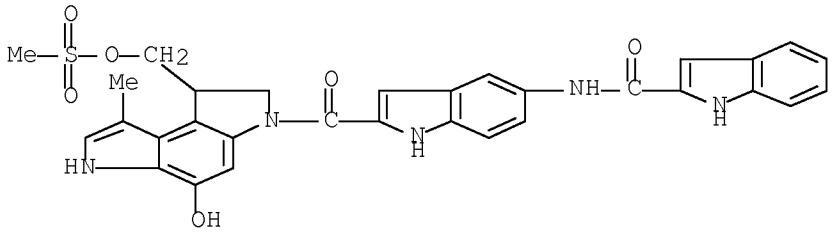
II

AB Title compds. I and II (R1, R2, R3 = H, alkyl, phenyl; R4 = H, acyl; R5 = acyl; R6 = halo, substituted sulfonyloxy; R7 = Me, substituted Me) and their salts, useful as UV light absorbents, bactericides, and antitumors were prepd.

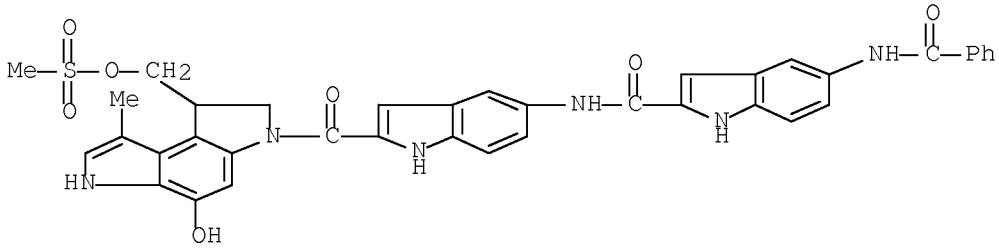
Thus, II (R1 = R2 = R3 = H, R5 = mesyl, R7 = PhCH2) was N-demesylated, N-acetylated, O-mesylated, O-debenzylated, and cyclized to give I (R1 = R2 = R3 = H, R4 = Ac). The latter compd. showed cytotoxic activity against murine L1210 tumor cells at 0.0048 .mu.g/mL.

IT 101134-75-2P 101134-79-6P 101134-83-2P
101134-84-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)

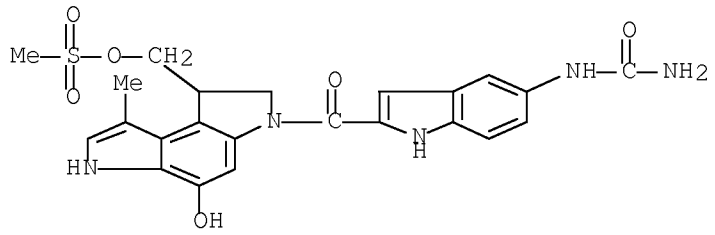
RN 101134-75-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



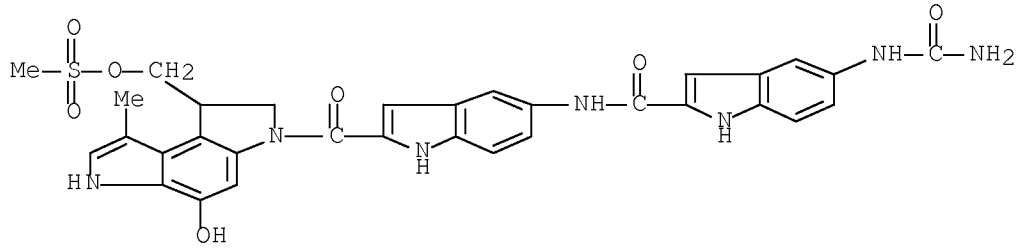
RN 101134-79-6 CAPLUS
CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



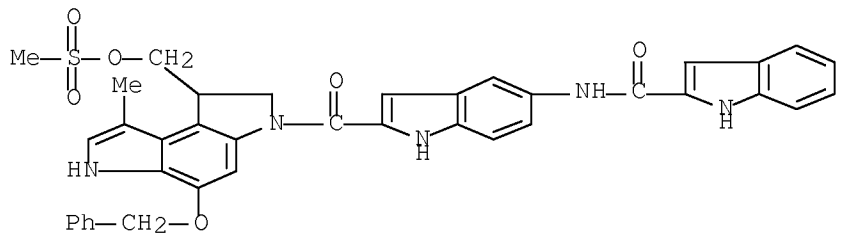
RN 101134-83-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-5-hydroxy-8-methyl-, .alpha.-methanesulfonate (9CI) (CA INDEX NAME)



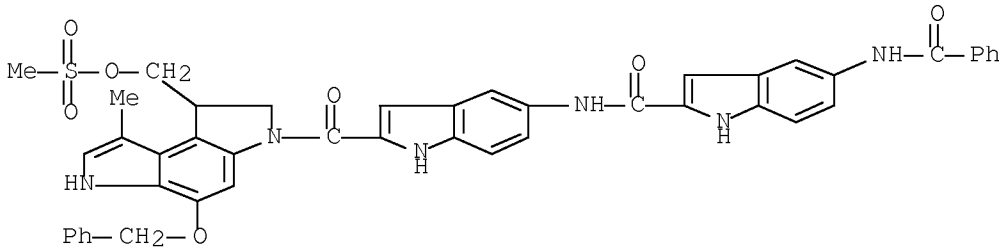
RN 101134-84-3 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-5-hydroxy-8-methyl-1-[[(methylsulfonyl)oxy]methyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



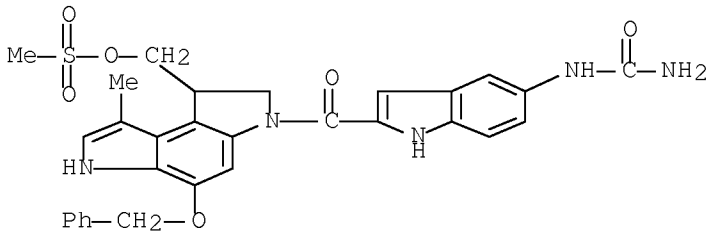
IT 101134-61-6P 101134-62-7P 101134-63-8P
101134-65-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzylation of)
RN 101134-61-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



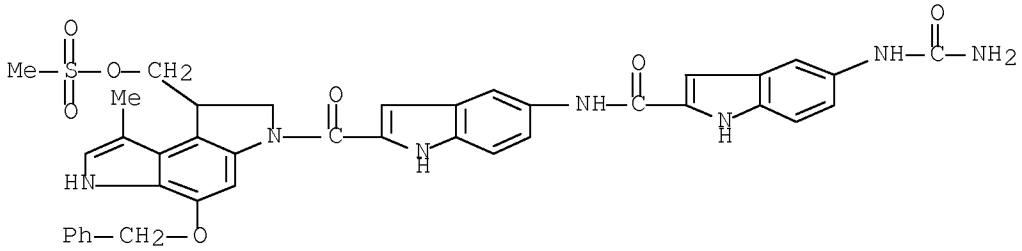
RN 101134-62-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



RN 101134-63-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-, methanesulfonate (ester) (9CI) (CA INDEX NAME)

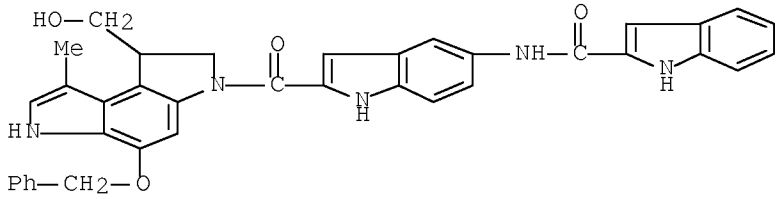


RN 101134-65-0 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

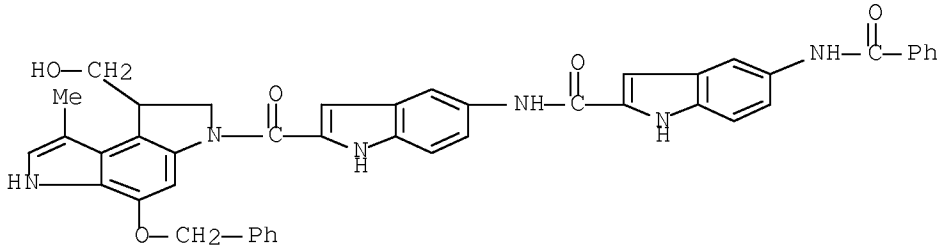


IT 101134-50-3P 101134-52-5P 101134-53-6P
101151-43-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and mesylation of)

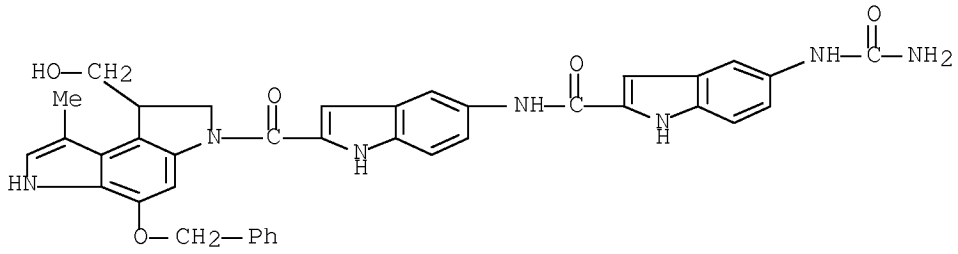
RN 101134-50-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



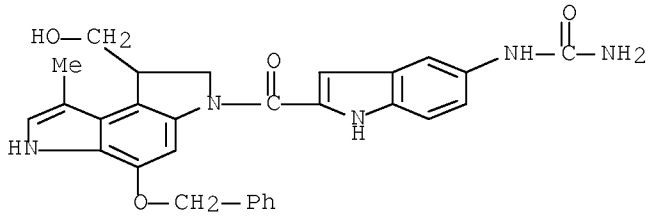
RN 101134-52-5 CAPLUS
CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



RN 101134-53-6 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[[1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

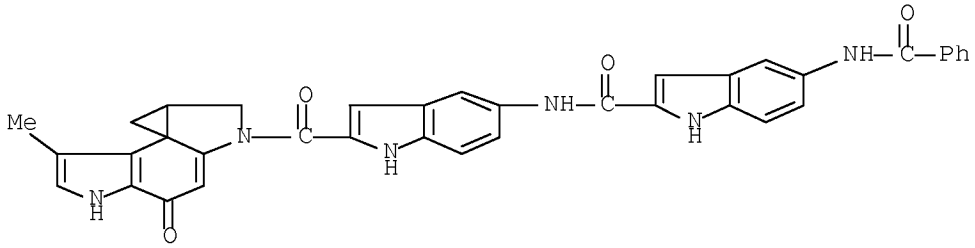


RN 101151-43-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

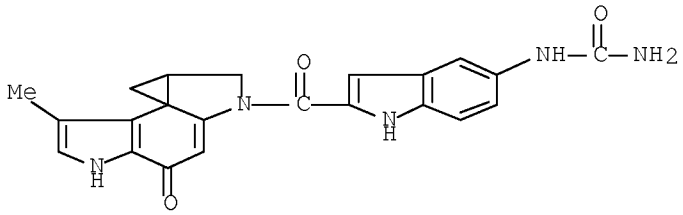


IT 101134-80-9P 101151-46-6P 101151-47-7P
101222-80-4P 104713-40-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antitumor and antibiotic)

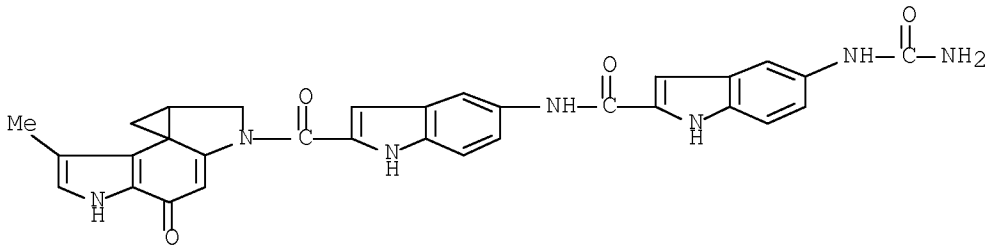
RN 101134-80-9 CAPLUS
CN 1H-Indole-2-carboxamide, 5-(benzoylamino)-N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



RN 101151-46-6 CAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, 2-[[5-[(aminocarbonyl)amino]-1H-indol-2-yl]carbonyl]-1,2,8,8a-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)

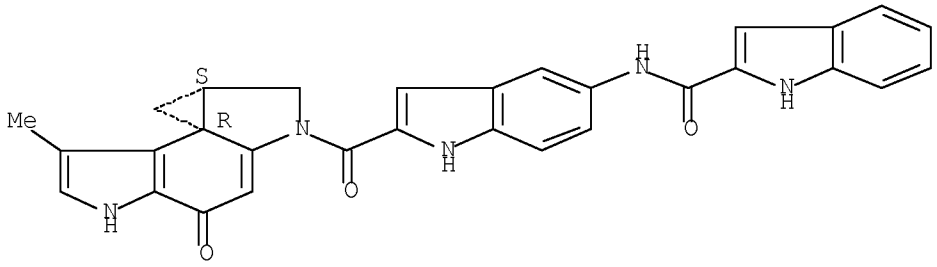


RN 101151-47-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(aminocarbonyl)amino]-N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

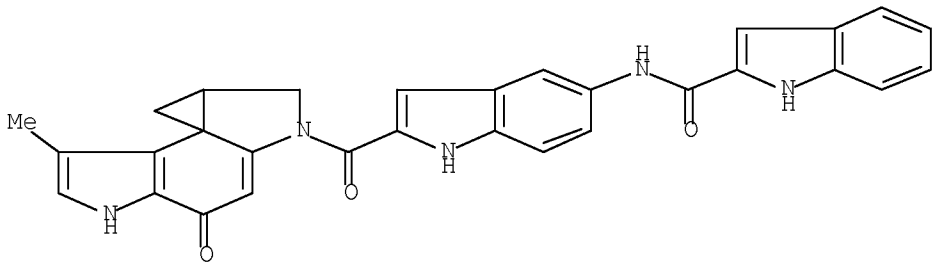


RN 101222-80-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(7bR,8aS)-4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 104713-40-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)carbonyl]-1H-indol-5-yl]- (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	56.73	248.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -7.20 -7.20

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DICTIONARY FILE UPDATES: 7 JUL 2008 HIGHEST RN 1032964-85-4

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experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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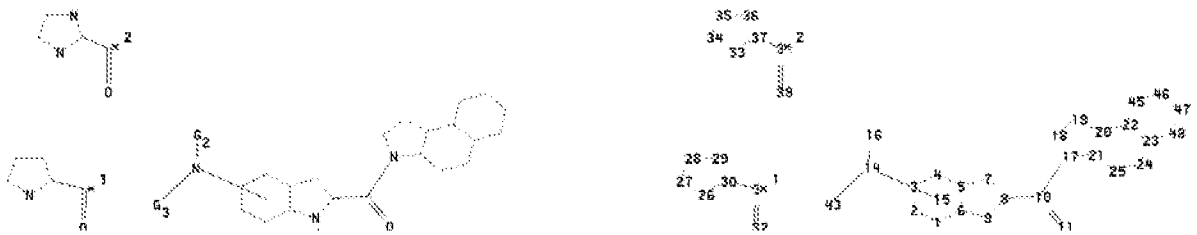

chain nodes :
10 11 13 14 16 31 32 38 39 43
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 22 23 24 25 26 27 28 29 30
33 34 35 36 37 45 46 47 48
chain bonds :
8-10 9-13 10-11 10-17 14-16 14-43 30-31 31-32 37-38 38-39
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-18 17-21 18-19 19-20 20-21
20-22 21-25 22-23 22-45 23-24 23-48 24-25 26-27 26-30 27-28 28-29 29-30
33-34 33-37
34-35 35-36 36-37 45-46 46-47 47-48
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-13 10-11 10-17 14-16 14-43
17-18 17-21 18-19 19-20 20-21 20-22 21-25 22-23 22-45 23-24 23-48 24-25

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26-27  26-30
27-28  28-29  29-30  31-32  33-34  33-37  34-35  35-36  36-37  38-39  45-46  46-47
47-48
exact bonds :
8-10  30-31  37-38
isolated ring systems :
containing 26 : 33 :


G2:H,CH,t-Bu

G3:[*1],[*2]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:CLASS
11:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom  22:Atom
23:Atom  24:Atom  25:Atom  26:Atom  27:Atom  28:Atom  29:Atom  30:Atom  31:CLASS
32:CLASS  33:Atom
34:Atom  35:Atom  36:Atom  37:Atom  38:CLASS  39:CLASS  43:CLASS  45:Atom  46:Atom
47:Atom
48:Atom




L8      STRUCTURE UPLOADED

=> d
L8 HAS NO ANSWERS
L8              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l8
SAMPLE SEARCH INITIATED 21:36:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      228 TO ITERATE

100.0% PROCESSED      228 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         3655 TO     5465
PROJECTED ANSWERS:               1 TO       80

L9            1 SEA SSS SAM L8

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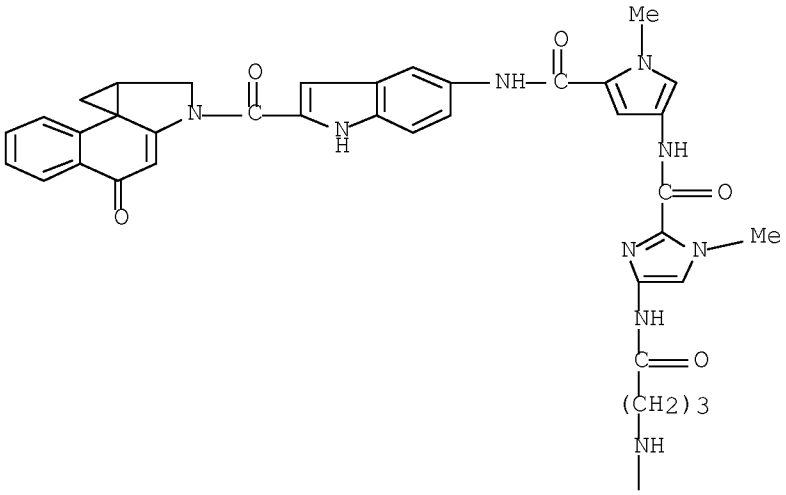

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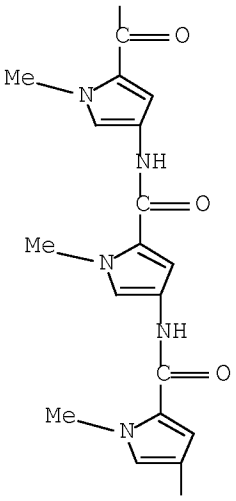

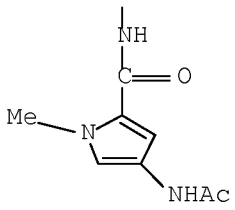

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=> s l10
L11 16 L10

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L11 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:492970 CAPLUS Full-text
TITLE: Sequence-specific alkylation by Y-shaped and tandem hairpin pyrrole-imidazole polyamides
AUTHOR(S): Sasaki, Shunta; Bando, Toshikazu; Minoshima, Masafumi; Shinohara, Ken-ichi; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Kyoto University, Kitashirakawa-Oiwaketyo, Sakyo, Kyoto, 606-8502, Japan
SOURCE: Chemistry--A European Journal (2008), 14(3), 864-870
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To extend the target DNA sequence length of the hairpin pyrrole-imidazole (Py-Im) polyamide 1, the authors designed and synthesized Y-shaped and tandem hairpin Py-Im polyamides 2 and 3, which possess 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) as DNA-alkylating moieties. High-resoln. denaturing polyacrylamide gel electrophoresis by using 5'-Texas-Red-labeled 465 base pair (bp) DNA fragments revealed that conjugates 2 and 3 alkylated the adenine of the target DNA sequences at nanomolar concns. Conjugate 2 alkylated adenine N3 at the 3' end of two 8 bp match sequences, 5'-AA- TAACCA-3' (site A) and 5'-AAATTC-CA-3' (site C), while conjugate 3 recognized one 10 bp match sequence, 5'-AGAATAACCA-3' (site A) in the 465 bp DNA fragments. These results demonstrate that seco-CBI conjugates of Y-shaped and tandem hairpin polyamides have extended their target alkylation sequences.
IT INDEXING IN PROGRESS
IT 1032252-71-3P 1032252-73-5P 1032252-75-7P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase prepn. of tandem hairpin pyrrole-imidazole polyamides, evaluation of their DNA-alkylating capabilities and cytotoxicity in human cancer cell lines)
RN 1032252-71-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

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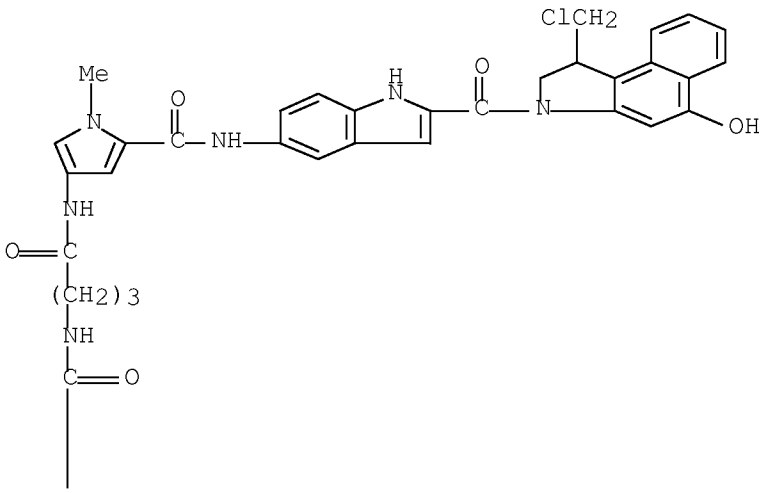

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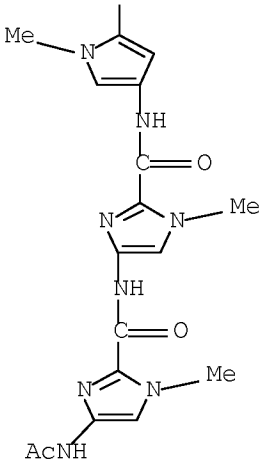

RN 1032252-73-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

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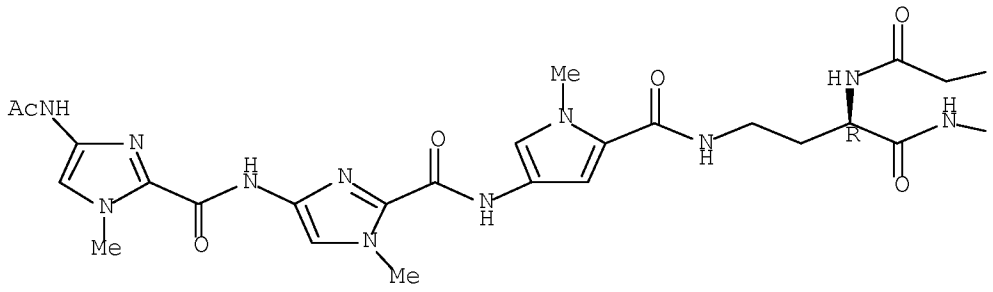

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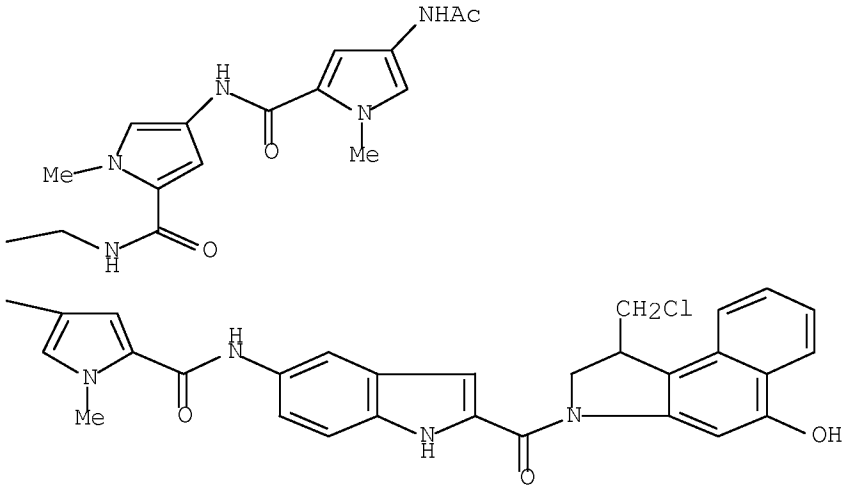

RN 1032252-75-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

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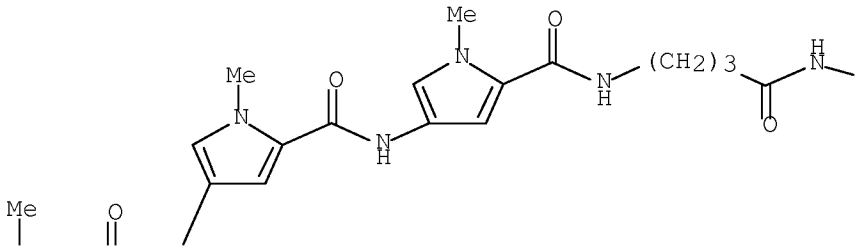

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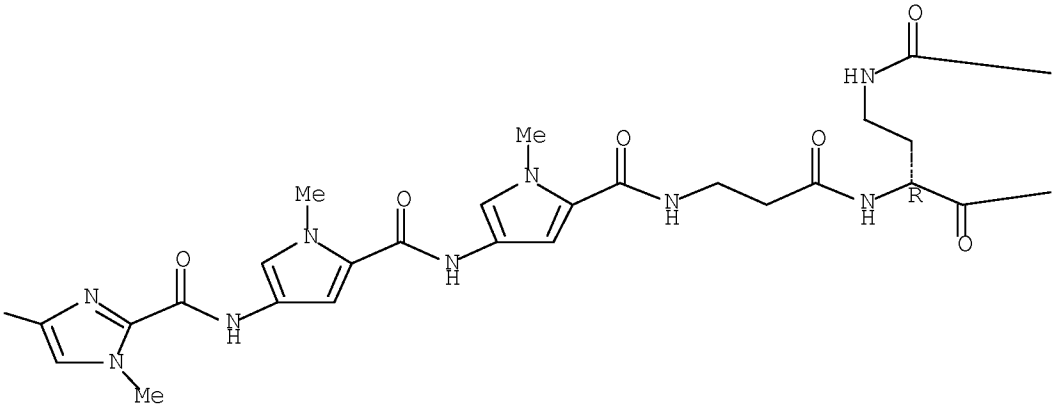

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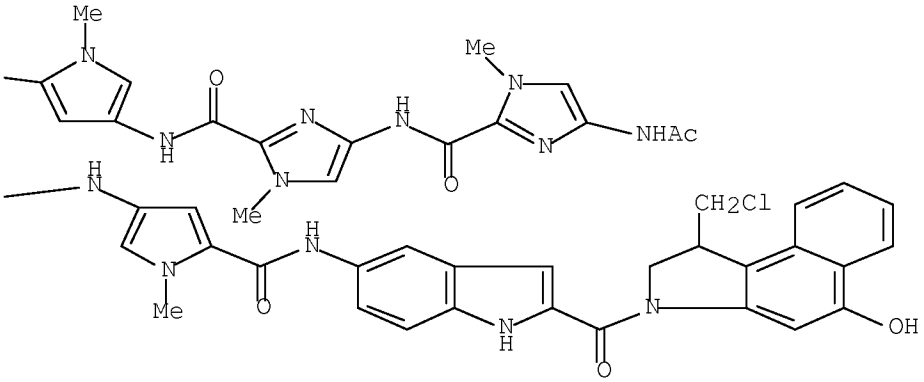

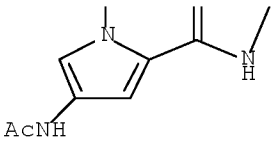

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:339576 CAPLUS Full-text
DOCUMENT NUMBER: 148:555820
TITLE: Requirement of .beta.-alanine components in sequence-specific DNA alkylation by pyrrole-imidazole conjugates with seven-base pair recognition
AUTHOR(S): Bando, Toshikazu; Minoshima, Masafumi; Kashiwazaki, Gengo; Shinohara, Ken-ichi; Sasaki, Shunta; Fujimoto, Jun; Ohtsuki, Akimichi; Murakami, Masataka; Nakazono, Satomi; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto, 606-8501, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2008), 16(5), 2286-2291
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To investigate the effect of incorporation of .beta.-alanine in alkylating N-methylpyrrole (Py)-N-methylimidazole (Im) polyamide, seco-CBI conjugates 2-8 were synthesized by an Fmoc solid-phase method and subsequent coupling with an alkylating moiety. DNA-alkylating activities of conjugates 2-8 were evaluated by high-resoln. denaturing gel electrophoresis with 202-base pair (bp) DNA fragments. Alkylation by conjugates 2 and 3, which have antiparallel pairings of .beta.-alanine (.beta.) opposite .beta. (.beta./.beta.) and Py/.beta., occurred mainly at the adenine (A) of the matching sequences, 5'-AGCTCC-3' (site 1) and 5'-AGCACC-3' (site 3). However, conjugate 4, with .beta./Py, did not show any DNA-alkylating activities. Similarly, conjugate 5, which possessed a Py/Py pair, weakly alkylated the matching sites at micromolar concns. Conjugates 6 and 7, which possessed .beta./.beta. and Py/.beta. pairs, resp., alkylated at the A of the matching sequences, 5'-ACTACC-3' (site 2) and 5'-ACAACC-3' (site 4). In contrast, conjugated 8, with a Py/Py pair, showed lower activity and less alkylated DNA at sites 2 and 4 with mismatched alkylation at site 1 at a higher concn. than that of 6 and 7. These results demonstrate that incorporation of .beta.-alanine is required for the sequence-specific alkylation by seco-CBI Py-Im conjugates with a seven-base pair sequence.

IT 865113-72-0P 1026780-48-2P 1026780-50-6P
1026780-52-8P 1026780-53-9P 1026780-54-0P
RL: BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP

(Preparation); RACT (Reactant or reagent)
(requirement of .beta.-alanine components in sequence-specific DNA alkylation by pyrrole-imidazole conjugates with seven-base pair recognition)

RN 865113-72-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

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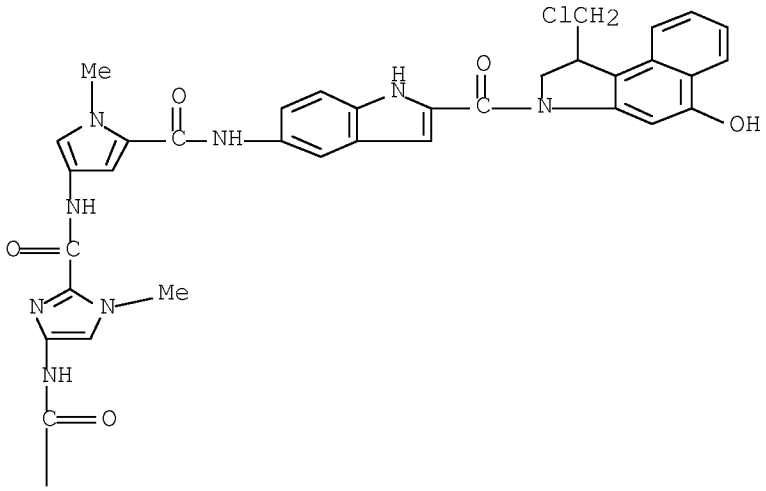

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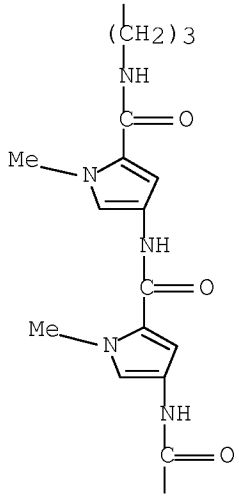

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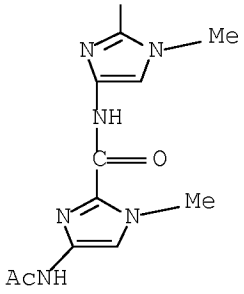

RN 1026780-48-2 CAPLUS
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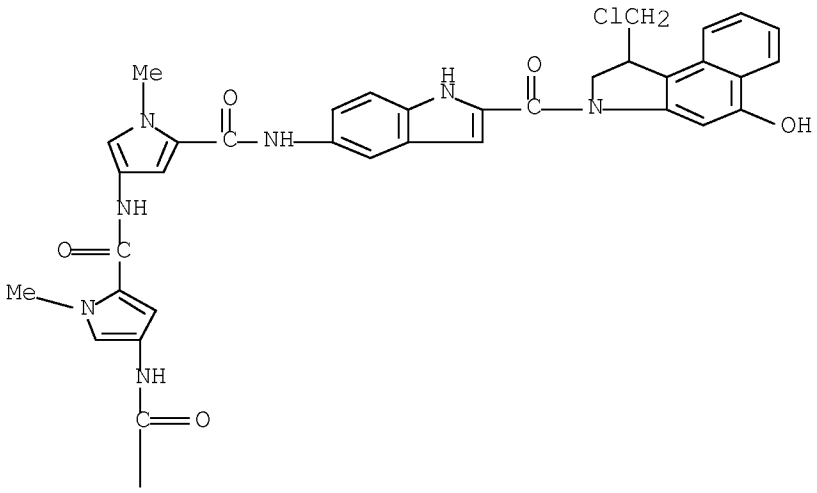

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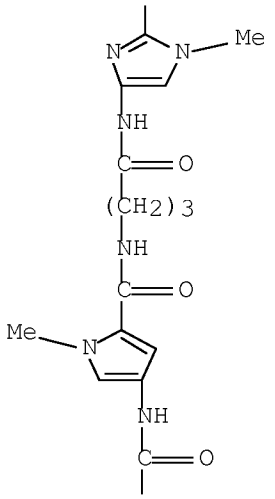

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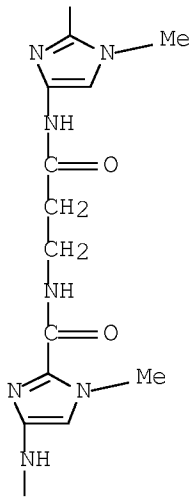

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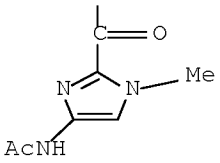

RN 1026780-50-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

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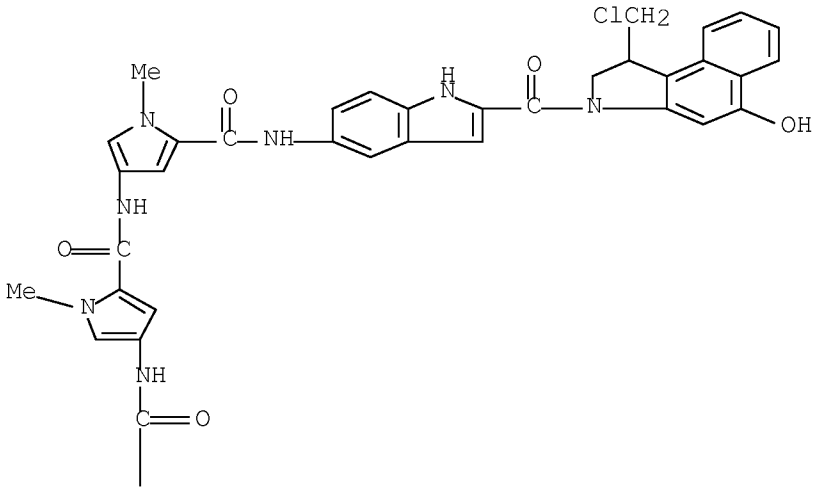

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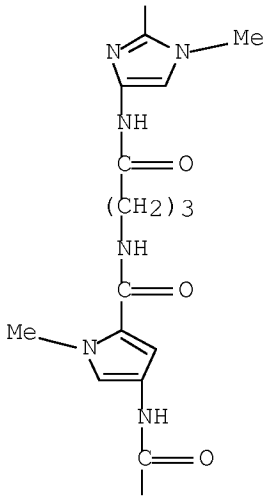

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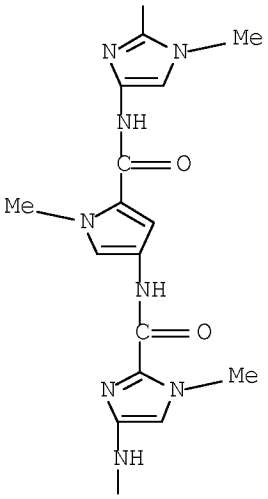

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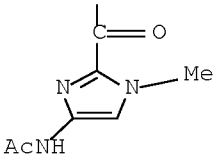

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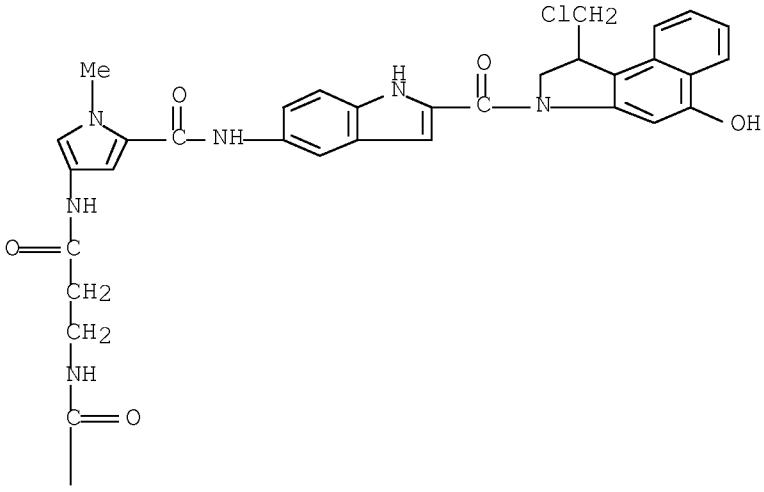

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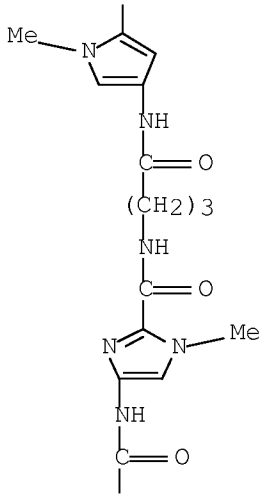

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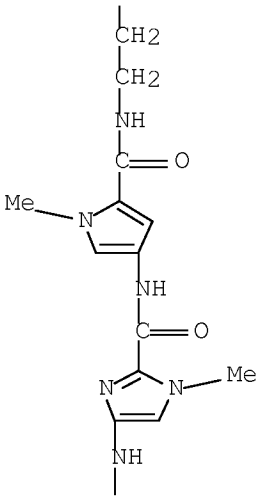

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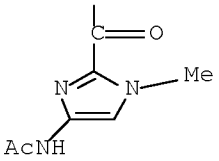

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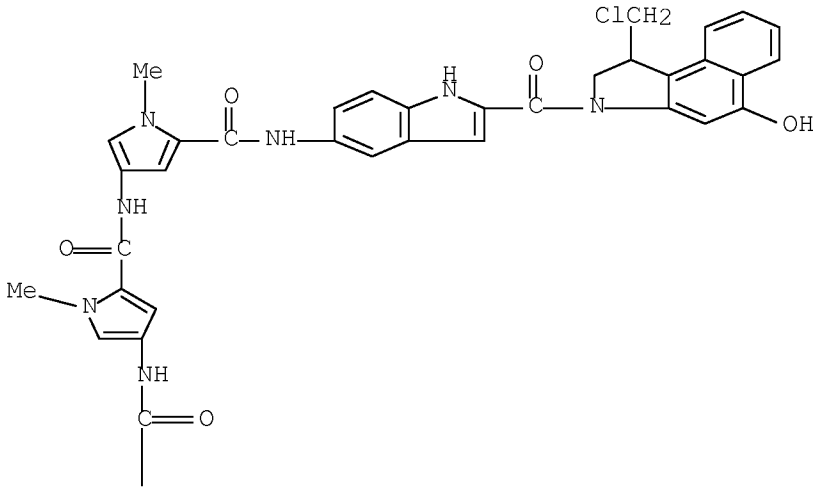

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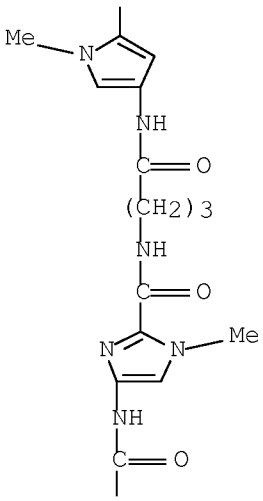

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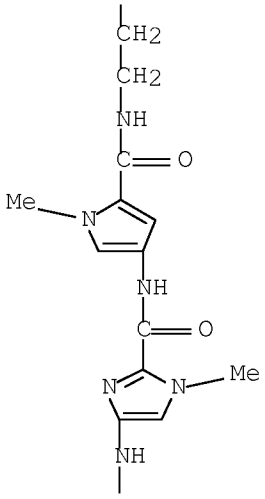

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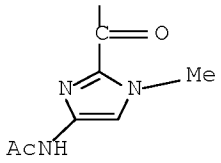

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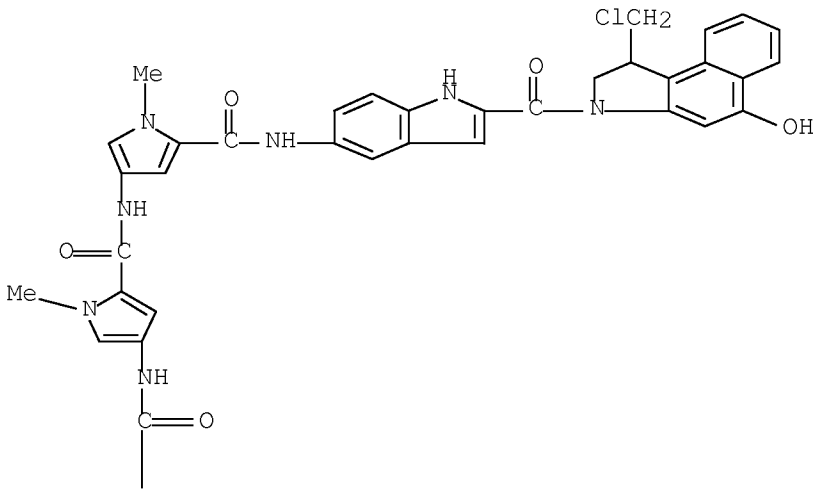

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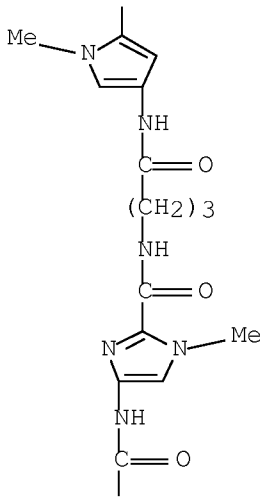

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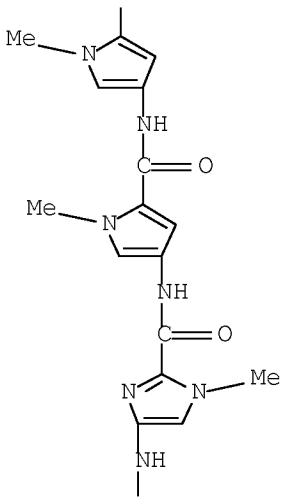

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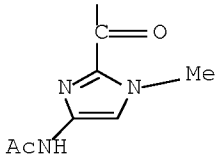

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L11 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:662474 CAPLUS Full-text
DOCUMENT NUMBER: 147:323219
TITLE: Molecular design of DNA alkylating pyrrole-imidazole polyamides with longer recognition sequence
AUTHOR(S): Minoshima, Masafumi; Sasaki, Shunta; Shinohara, Ken-ichi; Shimizu, Tatsuhiko; Bando, Toshikazu; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa-oiwakecho, Sakyo, Kyoto, 606-8502, Japan
SOURCE: Nucleic Acids Symposium Series (2006), (50), 165-166
CODEN: NASSCJ
URL: http://nass.oxfordjournals.org/content/vol50/issue1/index.dtl
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The sequence-specificity, and DNA alkylating activity of the conjugate 1, which consists of N-methylpyrrole (Py)-N-methylimidazole (Im) polyamides, 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) with indole

linker, were investigated in the absence or presence of partner Py-Im polyamide 2. High-resoln. denaturing PAGE showed that the specificity of DNA alkylation by 1 modulated in the presence of partner 2. We found that sequence-specific DNA alkylation by 1 and 2 with 10 base pair (bp) match recognition sequence through heterodimer formation. This result indicates one possibility of DNA alkylation with longer recognition sequence by different two mols.

IT 947726-88-7

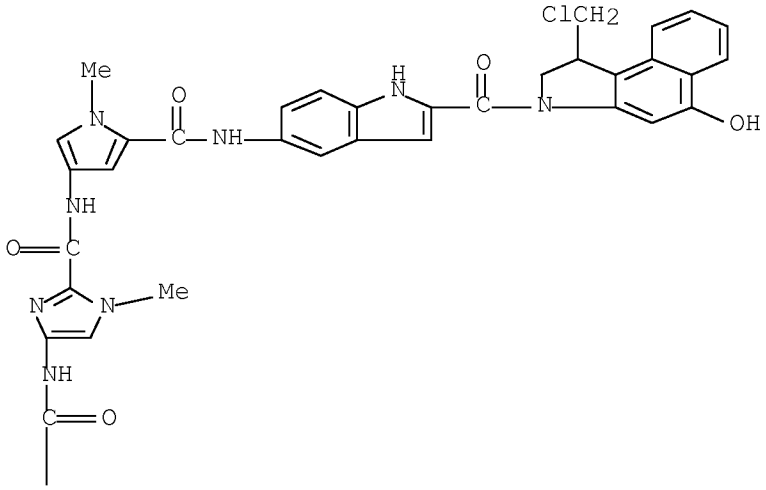
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(DNA alkylating agent; sequence-specific alkylation of DNA with pyrrole-imidazole polyamide seco-CBI conjugate in presence of partner polyamide)

RN 947726-88-7 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[3-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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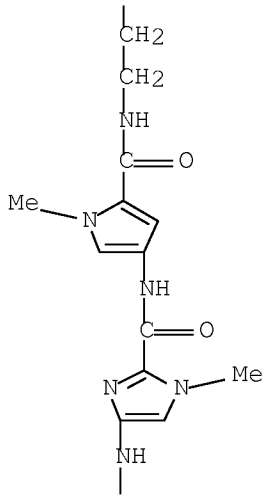

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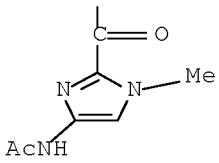

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L11 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:662469 CAPLUS Full-text
DOCUMENT NUMBER: 148:182769
TITLE: Synthesis and evaluation of sequence-specific DNA alkylating agents: effect of alkylation subunits
AUTHOR(S): Shimizu, Tatsuhiko; Sasaki, Shunta; Minoshima, Masafumi; Shinohara, Ken-ichi; Bando, Toshikazu; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa Oiwakecho, Sakyo-ku, Kyoto, 606-8502, Japan
SOURCE: Nucleic Acids Symposium Series (2006), (50), 155-156
CODEN: NASSCJ
URL: http://nass.oxfordjournals.org/content/vol50/issue1/index.dtl
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB We have demonstrated that hairpin pyrrole (Py)-imidazole (Im) polyamide-CBI conjugates selectively alkylate predetd. sequences. In this study, we investigated the effect of alkylation subunits, for example conjugates 1-4

with three types of DNA alkylating units, and Py-Im polyamides with indole linker. Conjugate 3 and 4 selectively alkylated the predetd. sequences as described previously, while conjugates 1 and 2 alkylate at mismatched sites.

IT 865113-72-0 1004312-35-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sequence-specific DNA alkylating agents as antitumor drugs with improved selectivity)

RN 865113-72-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

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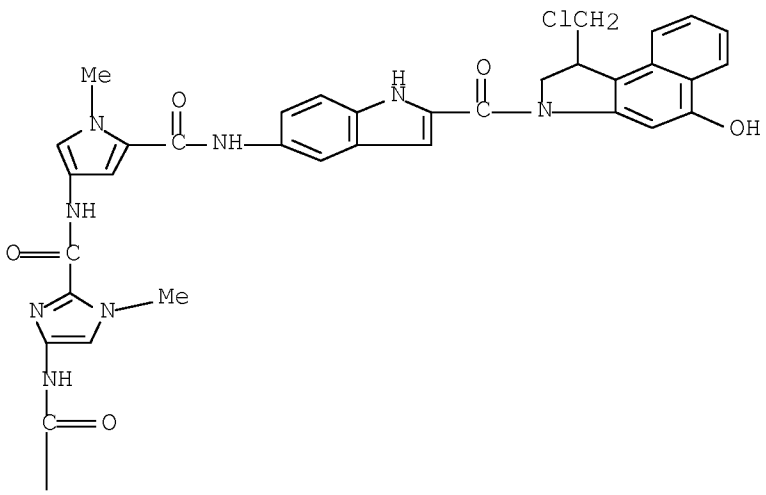

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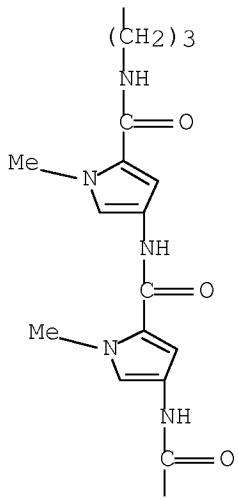

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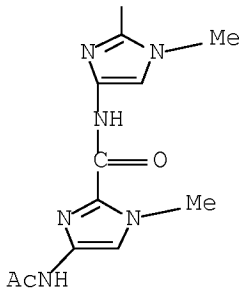

RN 1004312-35-9 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-(acetylamino)-N-[2-[[[5-[[[5-[[[4-[[5-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)

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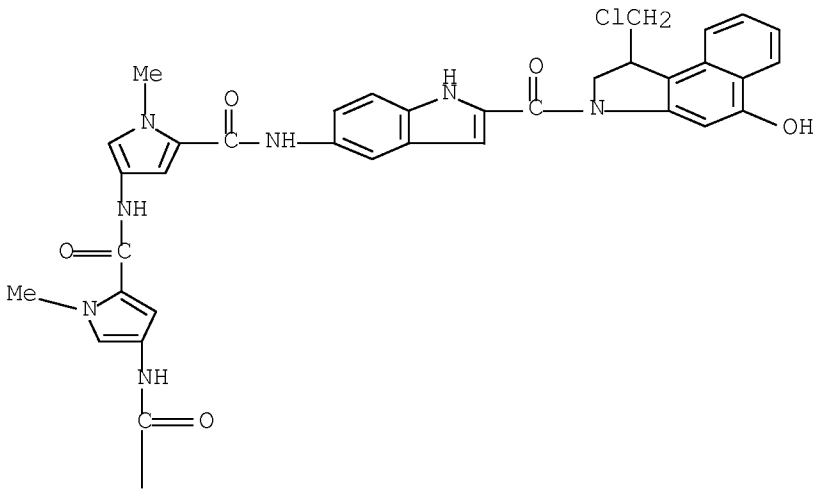

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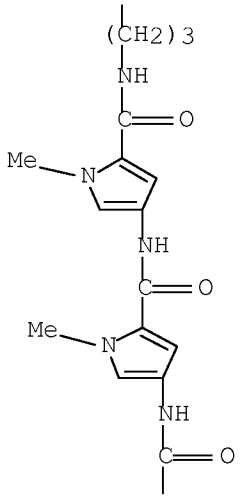

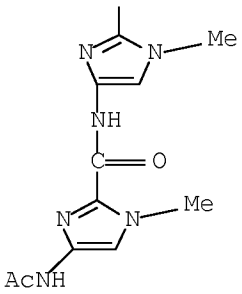

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L11 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:662447 CAPLUS Full-text
DOCUMENT NUMBER: 147:316628
TITLE: The biological impact of sequence-specific DNA alkylation by pyrroleimidazole polyamides
AUTHOR(S): Sasaki, Shunta; Minoshima, Masafumi; Shimizu, Tatsuhiko; Fujimoto, Jun; Shinohara, Ken-ichi; Bando, Toshikazu; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa Oiwake, Sakyo-ku, Kyoto, 606-8502, Japan
SOURCE: Nucleic Acids Symposium Series (2006), (50), 111-112
CODEN: NASSCJ
URL: http://nass.oxfordjournals.org/content/vol50/issue1/index.dtl
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB We have developed a series of novel DNA alkylating polyamides possessing indole linkers. Investigations using high-resoln. gel electrophoresis revealed that the indole linked Py-Im polyamide alkylated at A of a targeted nine base pair matching sequence. Evaluation in human cancer cell lines revealed that the indole linked Py-Im polyamides have strong cytotoxicities. Furthermore, we showed that alkylation of the template strand of the coding region by these polyamides causes effective gene silencing.

IT 893419-09-5P 947597-79-7P 947597-85-5P
947597-99-1P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(biol. impact of sequence-specific DNA alkylation by pyrroleimidazole polyamides)

RN 893419-09-5 CAPLUS
CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[3-[[5-[[[5-[[[2-[[[4-[[5-[[[5-[[[5-[[[3-[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

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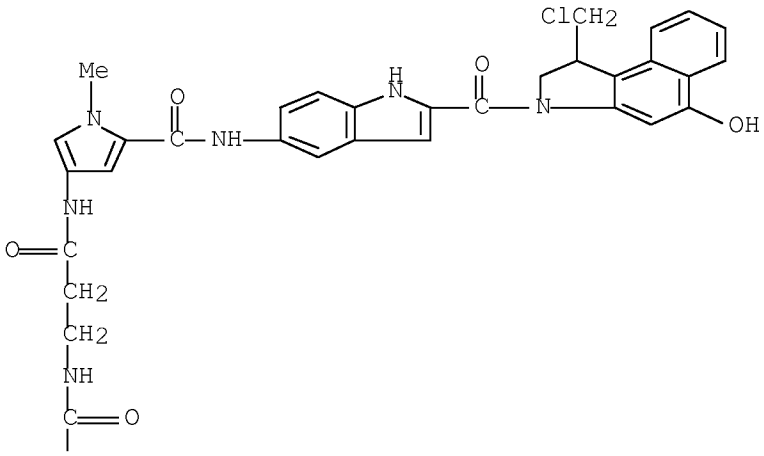

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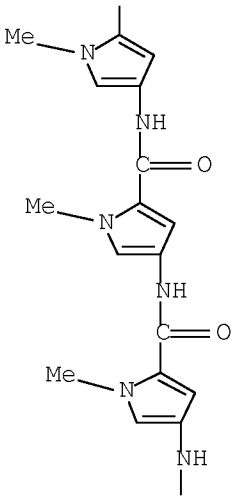

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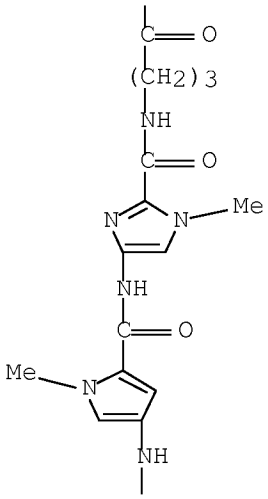

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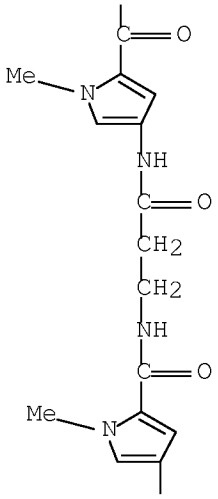

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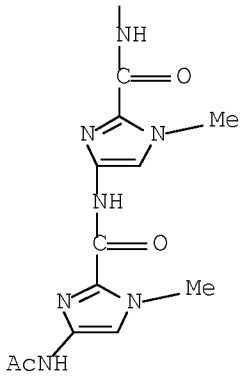

RN 947597-79-7 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-[[[4-[[[4-(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-N-[4-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]-1-methyl- (CA INDEX NAME)

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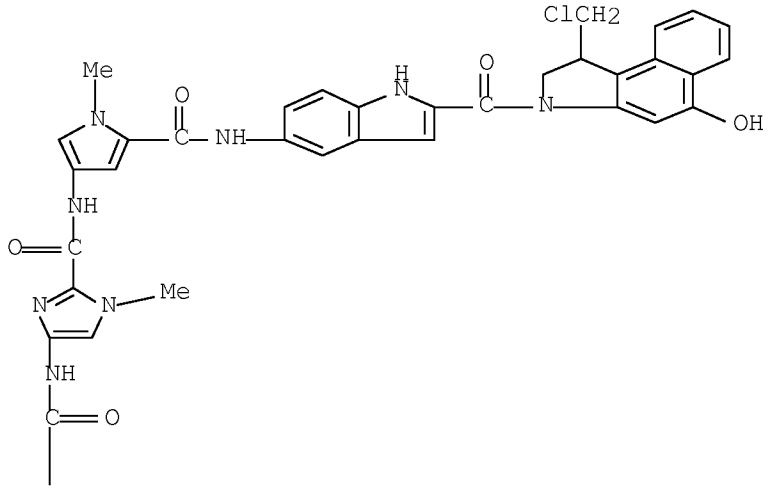

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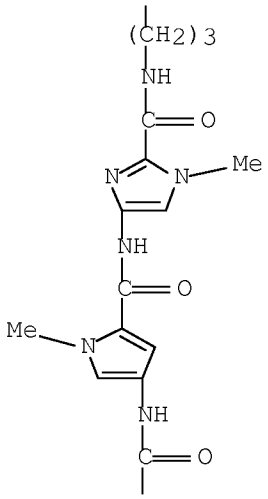

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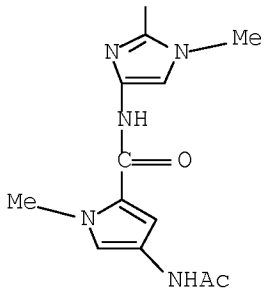
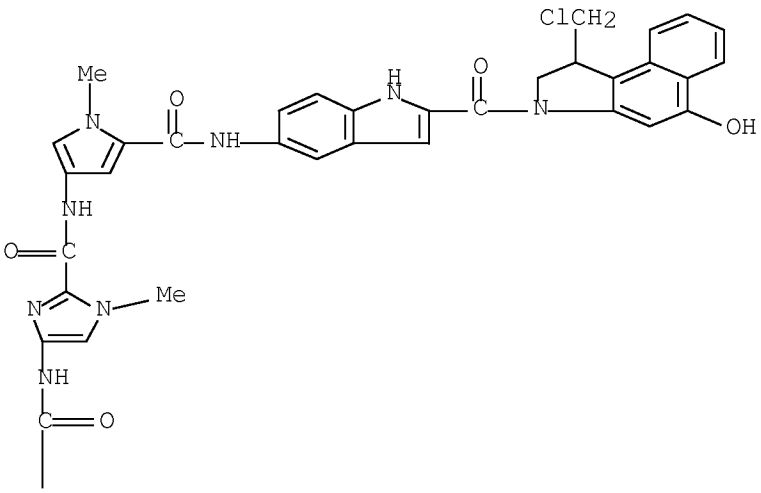


RN 947597-85-5 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-[[[4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-N-[4-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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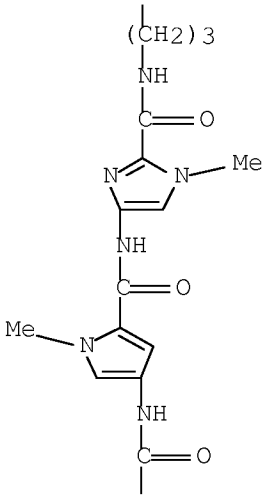

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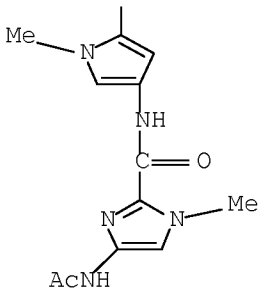

RN 947597-99-1 CAPLUS

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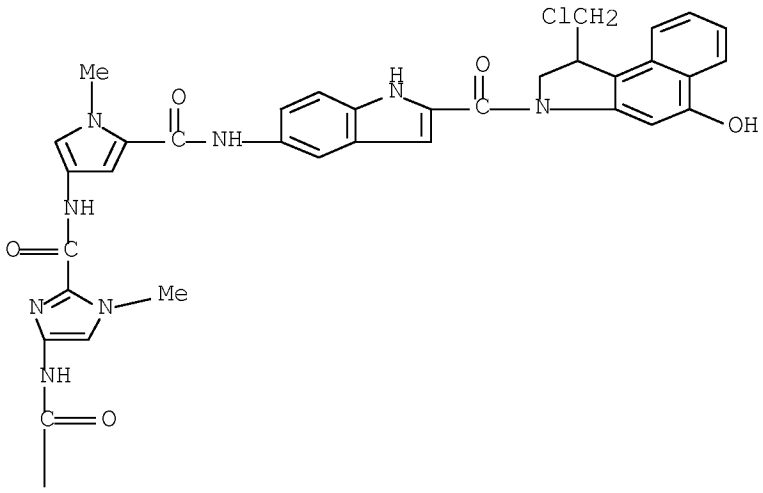

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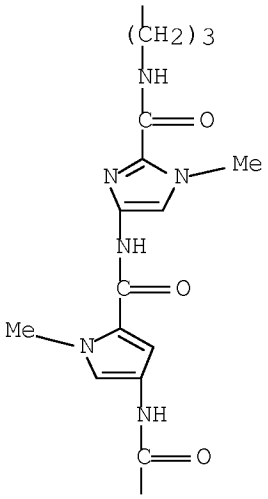

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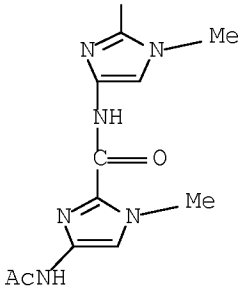

IT 947597-72-0P 947597-93-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(biol. impact of sequence-specific DNA alkylation by pyrroleimidazole polyamides)

RN 947597-72-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-[[[4-[[[4-(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-N-[4-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]-1-methyl- (CA INDEX NAME)

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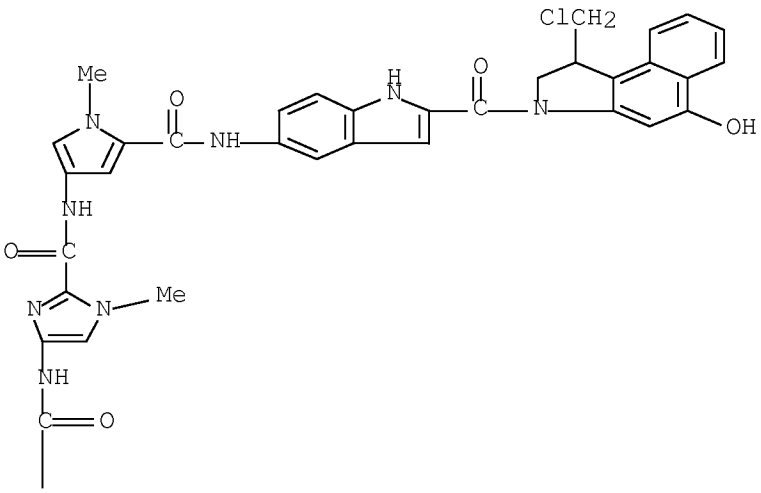

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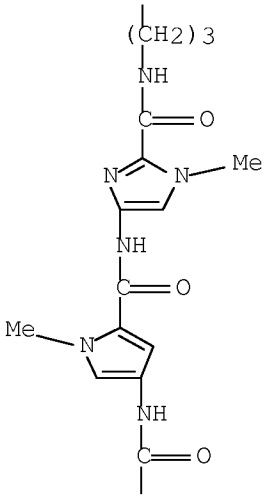

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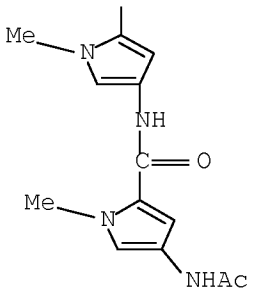

RN 947597-93-5 CAPLUS

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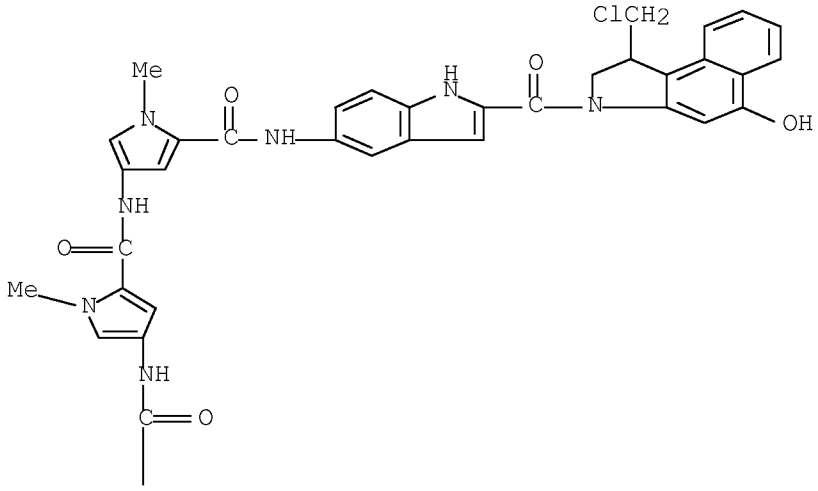

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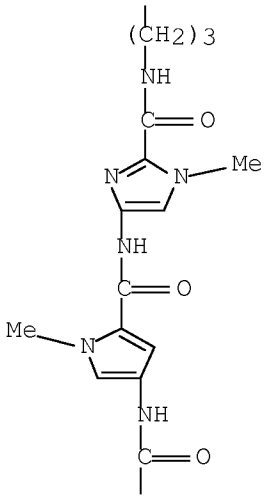

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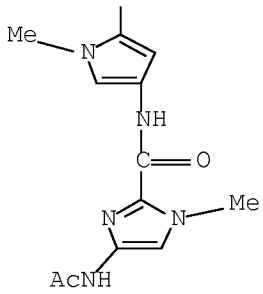

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L11 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:662248 CAPLUS Full-text
DOCUMENT NUMBER: 147:315627
TITLE: Sequence-specific gene silencing by alkylating Py-Im polyamide
AUTHOR(S): Shinohara, Ken-ichi; Sasaki, Shunta; Bando, Toshikazu; Sugiyama, Hiroshi
CORPORATE SOURCE: Graduate School of Science, Kyoto University, Kitashirakawa Oiwakecho, Sakyo-ku, Kyoto, 606-8502, Japan
SOURCE: Nucleic Acids Symposium Series (2005), (49), 75-76
CODEN: NASSCJ
URL: http://nass.oxfordjournals.org/content/vol49/issue1/index.dtl
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB We have demonstrated that hairpin pyrrole (Py)-imidazole (Im) polyamide-CPI conjugates selectively induced luciferase gene silencing by sequence-specific alkylation of the coding region. Recently, we developed a new type of Py-Im polyamide CBI conjugate with an indole linker as a stable sequence-specific alkylating agent. In this study, we investigated the gene silencing ability of polyamides A, B and C, which potentially target specific sequences in the promoter region, noncoding strand, and coding strand of the green fluorescent protein (GFP) gene, resp. The GFP vectors were transfected into human colon carcinoma cells (HCT116), and the cells treated with 100 nM of the polyamides for 24 h. Using direct observation of cell by fluorescence microscopy, a significant GFP-gene silencing effect was only seen with treatment with polyamide C. Polyamides A and B did not show such activity.

IT 865113-64-0 865113-67-3 885028-77-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequence-specific green fluorescent protein gene silencing in human cells by alkylating Py-Im polyamide)

RN 865113-64-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

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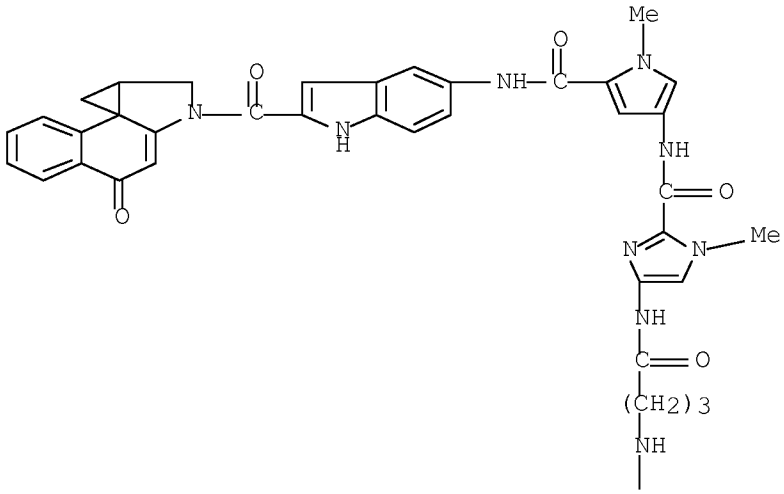

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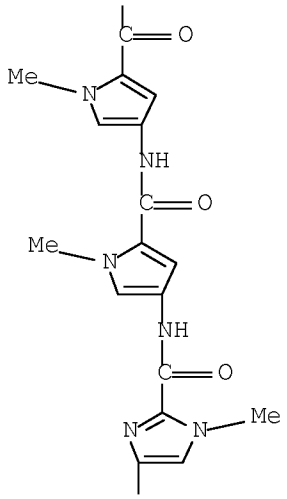

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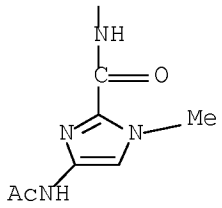

RN 865113-67-3 CAPLUS

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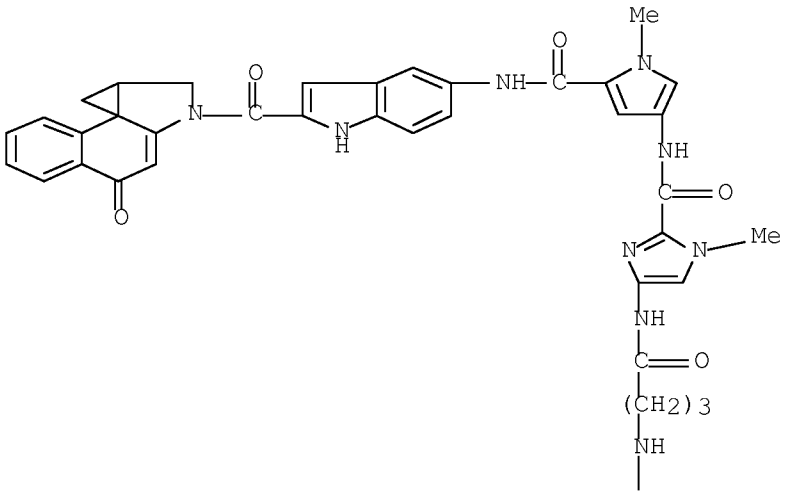
PAGE 1-A



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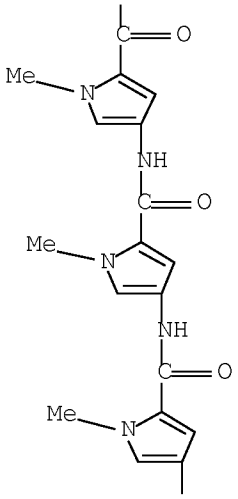

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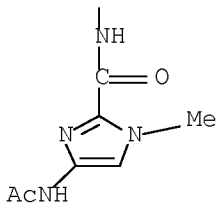

RN 885028-77-3 CAPLUS

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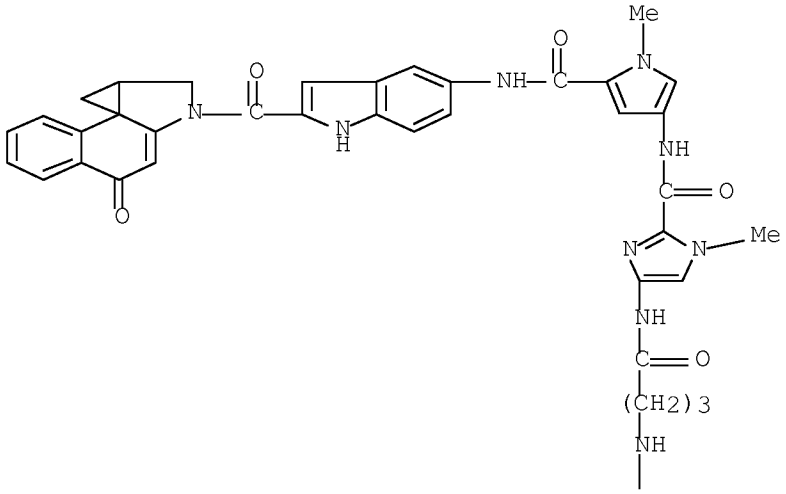
PAGE 1-A



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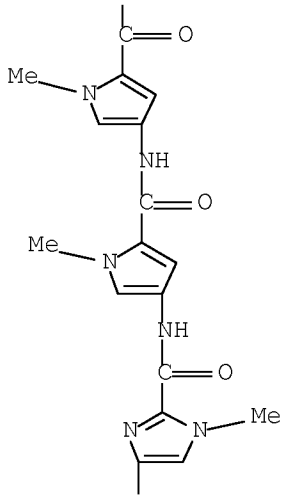
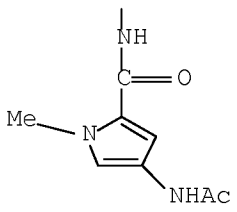




REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:662158 CAPLUS Full-text
DOCUMENT NUMBER: 148:517913
TITLE: Molecular design of alkylating pyrrole-imidazole polyamides with indole linker
AUTHOR(S): Sasaki, Shunta; Narita, Akihiko; Bando, Toshikazu; Sugiyama, Hiroshi
CORPORATE SOURCE: School of Biomedical Science, Tokyo Medical and Dental University, 2-3-10 Kanda-Surugadai, Chiyodaku, Tokyo, 101-0062, Japan
SOURCE: Nucleic Acids Symposium Series (2004), (48), 205-206
CODEN: NASSCJ
URL: http://nass.oxfordjournals.org/content/vol48/issue1/index.dtl
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

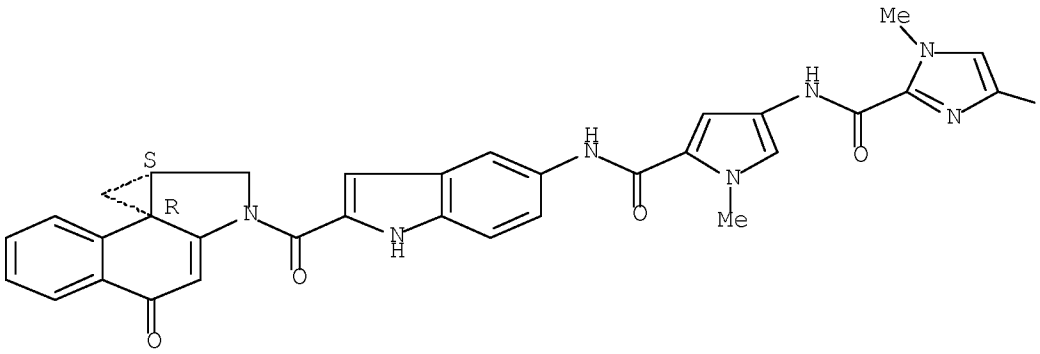
AB A series of novel DNA alkylating polyamide possessing indole linker was synthesized. The reactivities and specificities of these polyamides with double strand DNA were investigated by using high-resoln. gel electrophoresis. The results revealed that the indole linker linked Py-Im polyamides have the high alkylating activities and sequence specificities comparable to vinyl linker linked Py-Im polyamides.

IT 1021452-23-2P 1021452-26-5P 1021452-29-8P
1021452-32-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(mol. design of alkylating pyrrole-imidazole polyamides with indole linker)

RN 1021452-23-2 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



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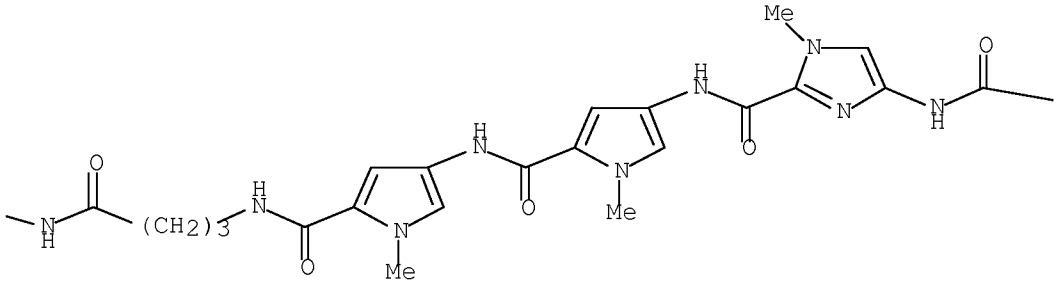

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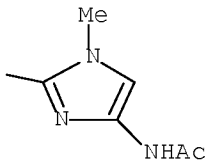
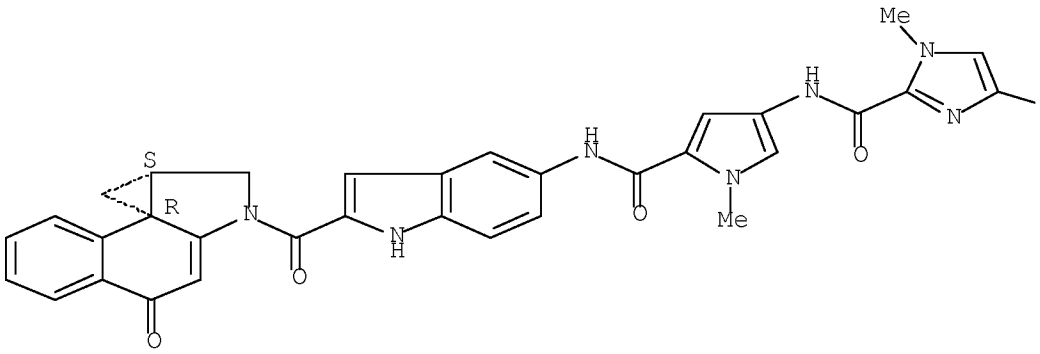


RN 1021452-26-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



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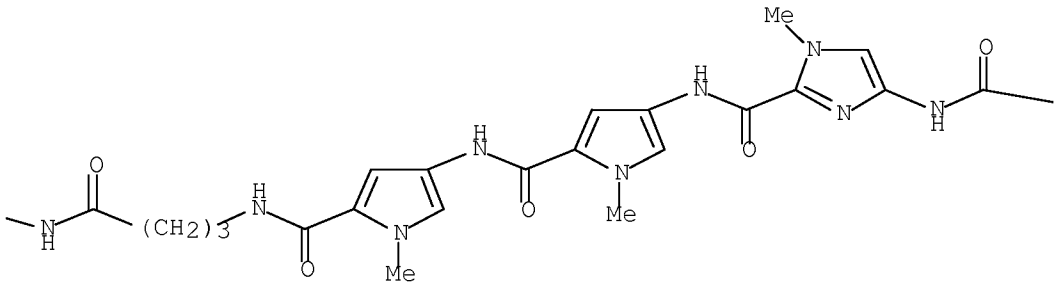

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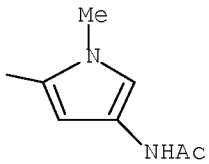
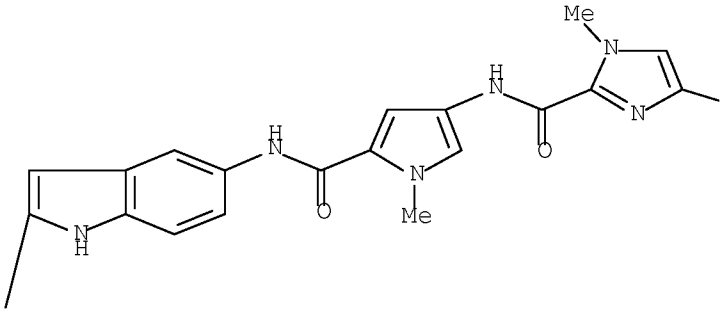


RN 1021452-29-8 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



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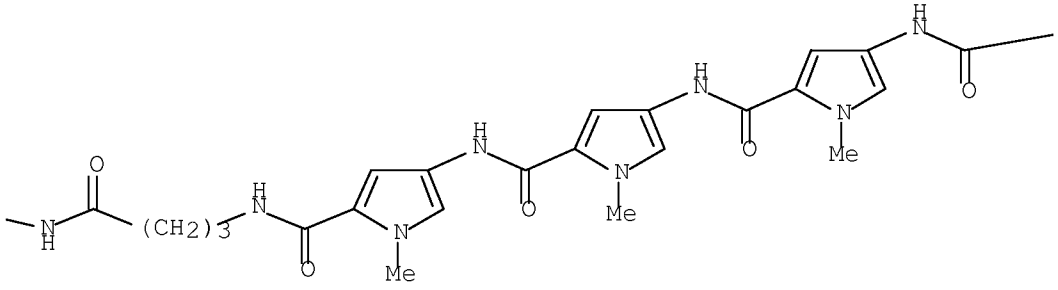

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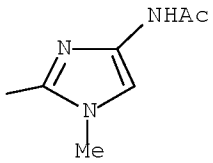

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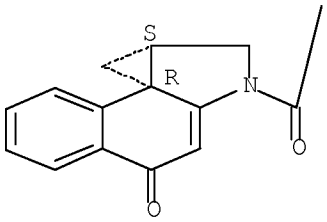
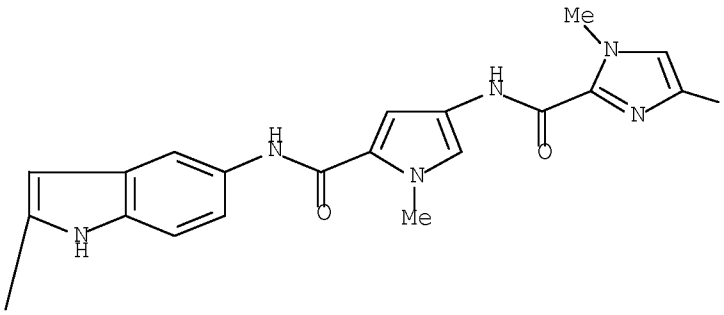


RN 1021452-32-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



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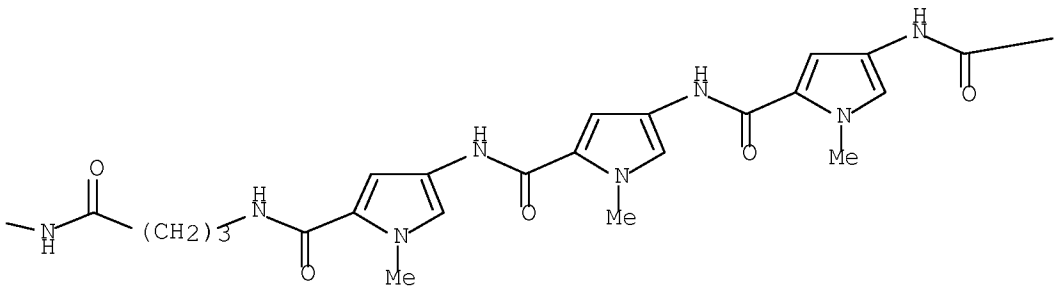

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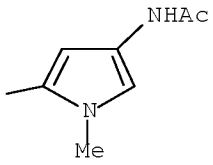

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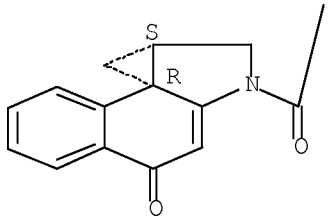


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:408268 CAPLUS Full-text
DOCUMENT NUMBER: 147:47403
TITLE: DNA Alkylation by Pyrrole-Imidazole seco-CBI Conjugates with an Indole Linker: Sequence-Specific DNA Alkylation with 10-Base-Pair Recognition through Heterodimer Formation
AUTHOR(S): Minoshima, Masafumi; Bando, Toshikazu; Sasaki, Shunta; Shinohara, Ken-ichi; Shimizu, Tatsuhiko; Fujimoto, Jun; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto, 606-8502, Japan
SOURCE: Journal of the American Chemical Society (2007), 129(17), 5384-5390
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:47403

AB The sequence-specific DNA alkylation by conjugates 4 and 5, which consist of N-methylpyrrole (Py)-N-methylimidazole (Im) polyamides and 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) linked with an indole linker, was investigated in the absence or presence of partner Py-Im polyamide 6. High-resoln. denaturing PAGE revealed that conjugate 4 alkylates DNA at the sequences 5'-(A/T)GCCTA-3' through hairpin formation, and alkylates 5'-GGAAAGAAAA-3' through an extended binding mode. However, in the presence of partner Py-Im polyamide 6, conjugate 4 alkylates DNA at a completely different sequence, 5'-AGGTTGTCCA-3'. Alkylation of 4 in the presence of 6 was effectively inhibited by a competitor 7. Surface plasmon resonance (SPR) results indicated that conjugate 4 does not bind to 5'-AGGTTGTCCA-3', whereas 6 binds tightly to this sequence. The results suggest that alkylation proceeds through heterodimer formation, indicating that this is a general way

to expand the recognition sequence for DNA alkylation by Py-Im seco-CBI conjugates.

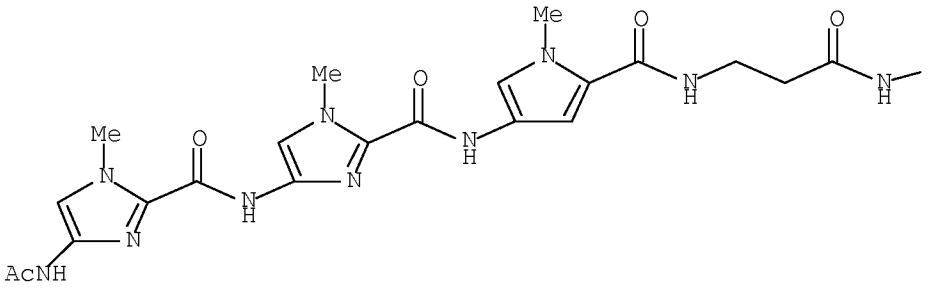
IT 939435-69-5P 939435-70-8P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(sequence-specific DNA alkylation by pyrrole-imidazole seco-CBI conjugates with an indole linker)

RN 939435-69-5 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[3-[[2-[[[5-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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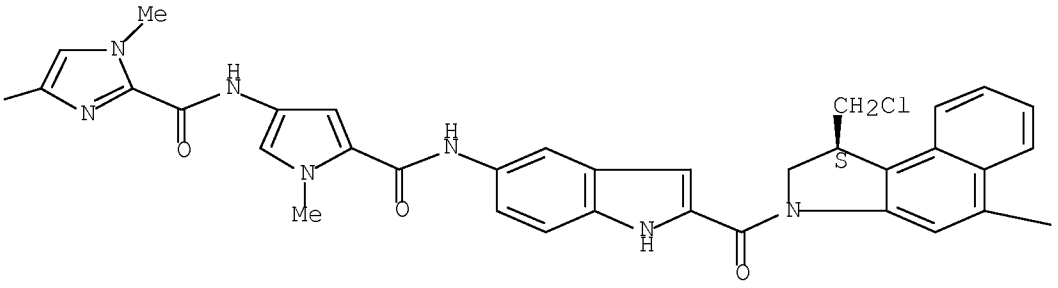

PAGE 1-C

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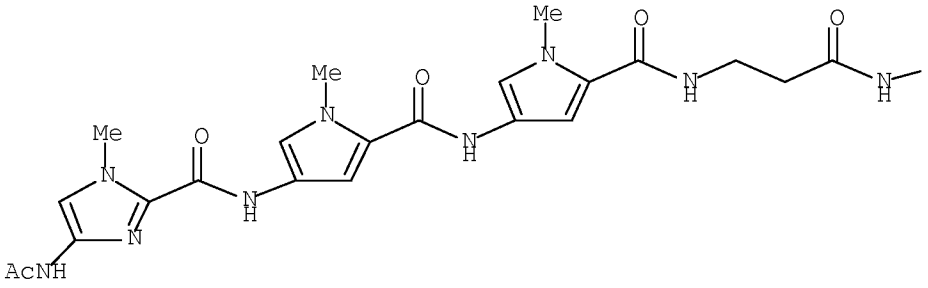
RN 939435-70-8 CAPLUS
CN 1H-Imidazole-2-carboxamide, 4-(acetylamino)-N-[5-[[[5-[[[3-[[2-[[[5-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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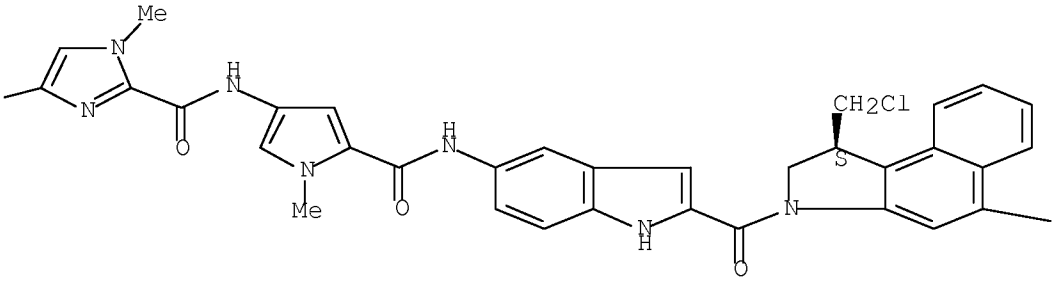

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L11 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:860352 CAPLUS Full-text
DOCUMENT NUMBER: 145:448749
TITLE: Sequence-Specific Alkylation of Double-Strand Human Telomere Repeat Sequence by Pyrrole-Imidazole Polyamides with Indole Linkers
AUTHOR(S): Sasaki, Shunta; Bando, Toshikazu; Minoshima, Masafumi; Shimizu, Tatsuhiko; Shinohara, Ken-Ichi; Takaoka, Toshiyasu; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kyoto, 606-8502, Japan
SOURCE: Journal of the American Chemical Society (2006), 128(37), 12162-12168
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:448749
GI

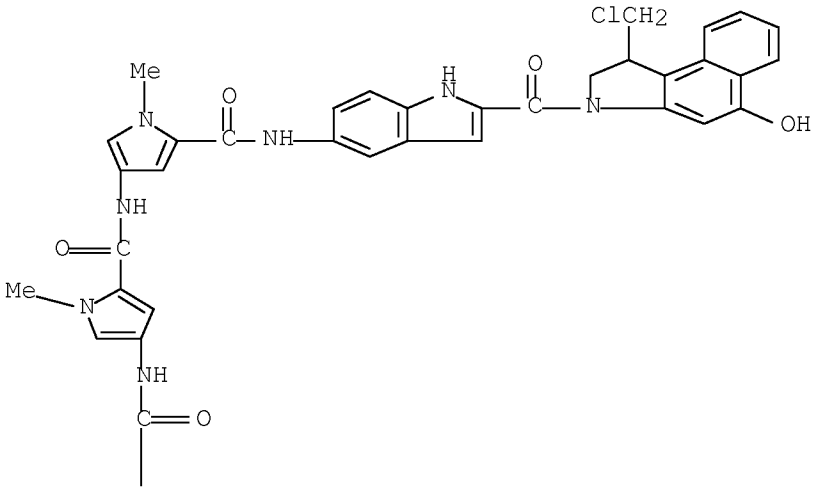
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The authors designed and synthesized pyrrole (Py)-imidazole (Im) hairpin polyamide 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) conjugates which target both strands of the double-stranded region of the human telomere repeat sequences, 5'-d(TTAGGG)n-3'/5'- d(CCCTAA)n-3'. High-resoln. denaturing PAGE demonstrated that the conjugates alkylated DNA at the 3' A of 5'-ACCCTA-3' and 5'-AGGGTTA-3', resp. Cytotoxicities of the conjugates were evaluated using 39 human cancer cell lines; avs. of log IC50 values for these conjugates were -6.96 (110 nM) and -7.24 (57.5 nM), resp. These conjugates have potential as antitumor drugs capable of targeting telomere repeat sequence.

IT 865113-70-8P 912562-39-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sequence-specific alkylation of double-strand human telomere repeat sequence by pyrrole-imidazole polyamides with indole linkers)
RN 865113-70-8 CAPLUS
CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-

yl]carbonyl]amino]-N-[2-[[[4-[[5-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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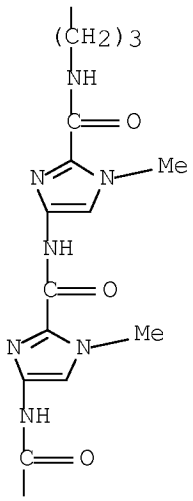

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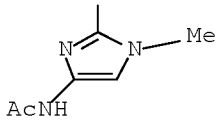
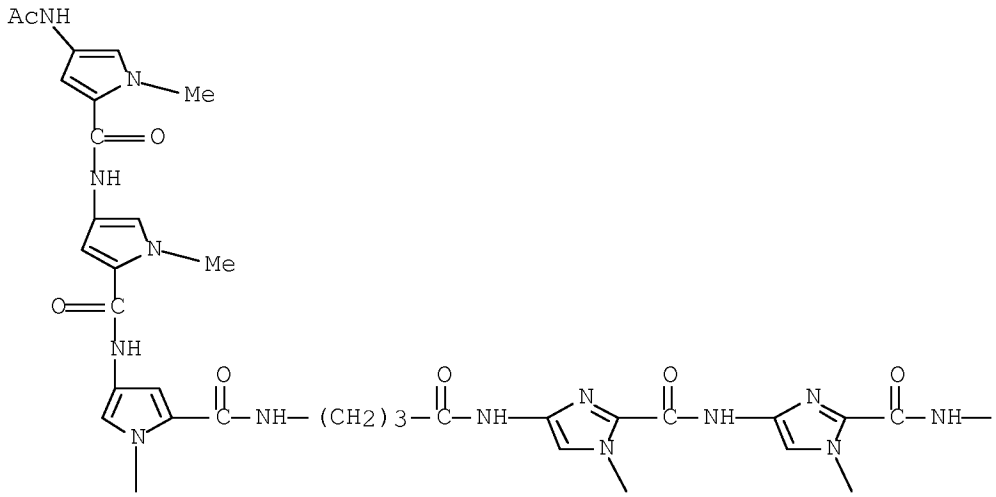


RN 912552-39-7 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-[[4-[[[4-[[[4-[[[4-(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-oxobutyl]amino]-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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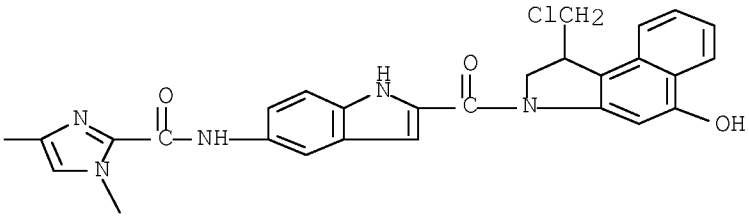


PAGE 2-A

Me Me Me

PAGE 2-B

Me

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:385992 CAPLUS Full-text

DOCUMENT NUMBER: 145:103905

TITLE: Efficient DNA Alkylation by a Pyrrole-Imidazole CBI Conjugate with an Indole Linker: Sequence-Specific Alkylation with Nine-Base-Pair Recognition

AUTHOR(S): Bando, Toshikazu; Sasaki, Shunta; Minoshima, Masafumi; Dohno, Chikara; Shinohara, Ken-Ichi; Narita, Akihiko; Sugiyama, Hiroshi

CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kyoto, 606-8501, Japan

SOURCE: Bioconjugate Chemistry (2006), 17(3), 715-720
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:103905

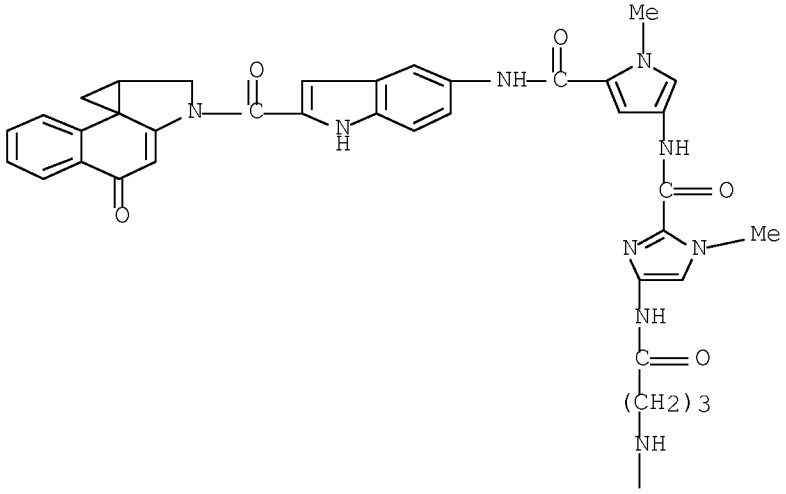
AB Conjugates of N-methylpyrrole (Py)-N-methylimidazole (Im) polyamides and 1,2,9,9a-tetrahydrocyclopropa[1,2-c]benz[1,2-e]indol-4-one (CBI) with a 5-amino-1H-indole-2-carbonyl linker were synthesized by Fmoc solid-phase synthesis and a subsequent liq.-phase coupling procedure. The DNA alkylating abilities of imidazole conjugates were examd. using Texas Red-labeled PCR fragments and high-resoln. denaturing gel electrophoresis. CBI conjugates exhibited highly efficient sequence-specific DNA alkylation comparable with previous CBI conjugates with a vinyl linker. Introduction of an indole linker greatly facilitated the synthesis of sequence-specific alkylating Py-Im polyamides.

IT 865113-64-0P 865113-66-2P 865113-72-0P
893419-09-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(DNA alkylation by pyrrole-imidazole hydrocyclopropabenzindolone conjugate with indole linker and sequence-specific alkylation with nine-base-pair recognition)

RN 865113-64-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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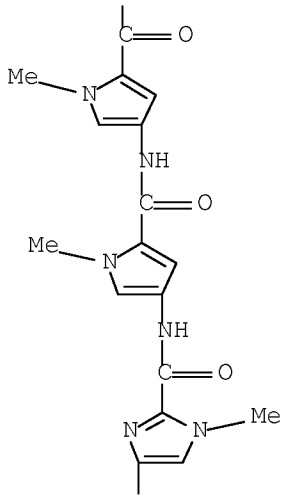

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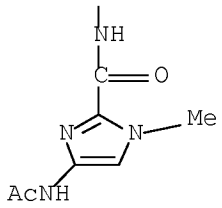

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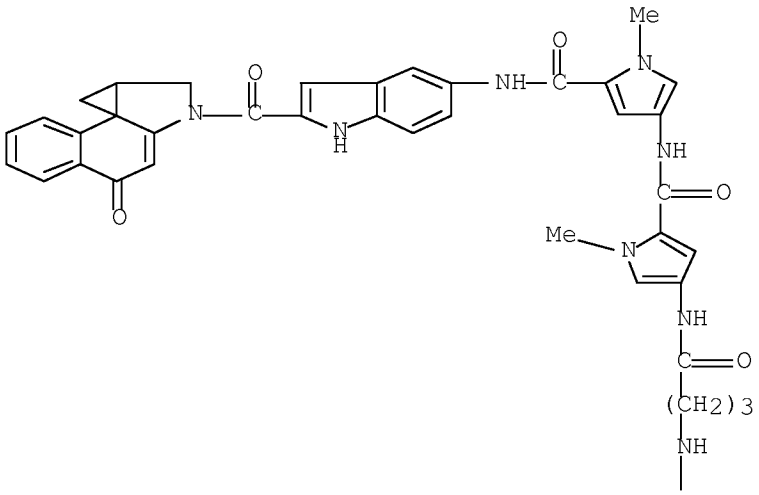

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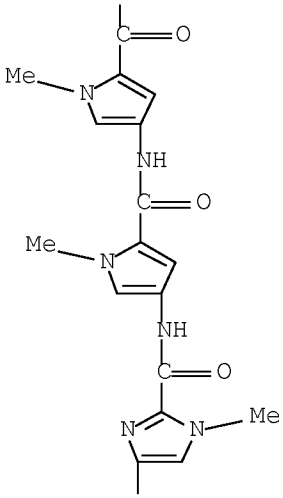

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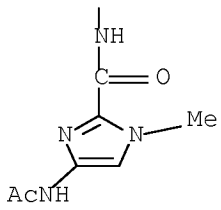

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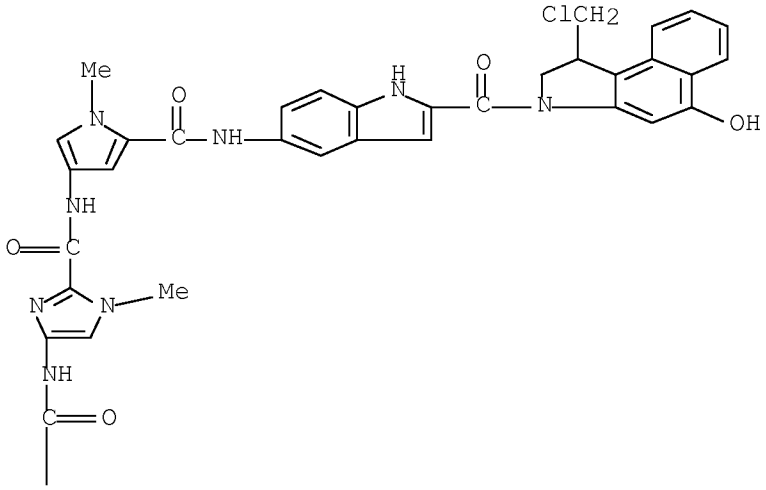

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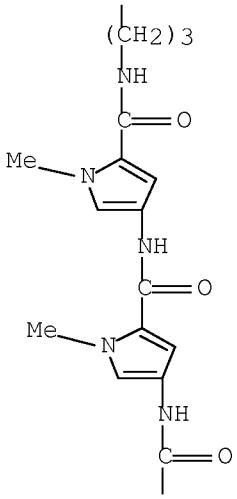

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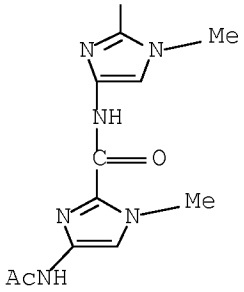

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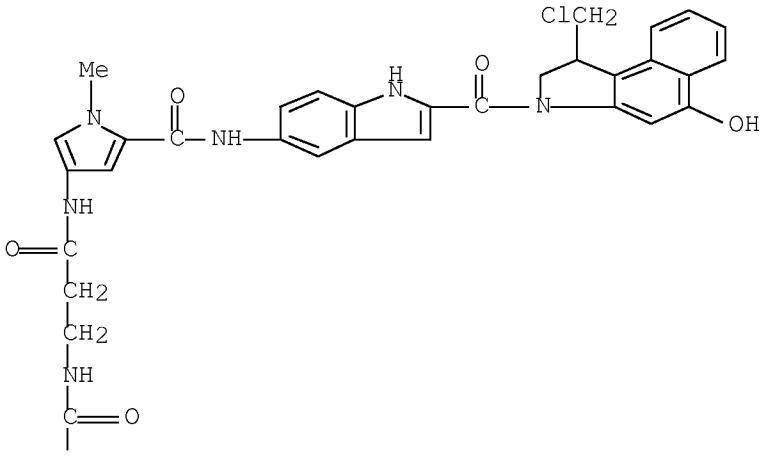

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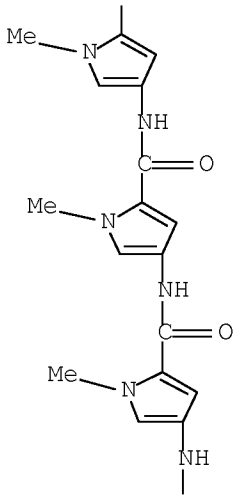

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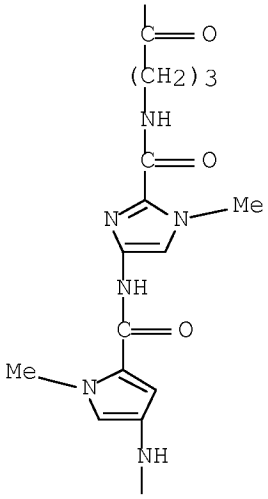

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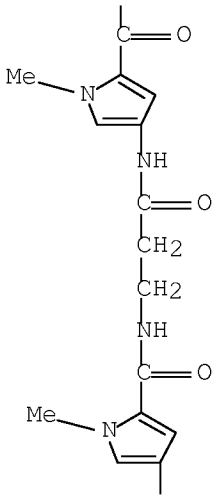

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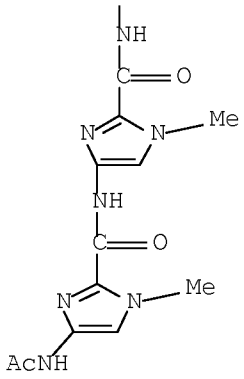


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:367591 CAPLUS Full-text

DOCUMENT NUMBER: 145:431752

TITLE: Antitumor activity of sequence-specific alkylating agents: pyrolle-imidazole CBI conjugates with indole linker

AUTHOR(S): Shinohara, Ken-ichi; Bando, Toshikazu; Sasaki, Shunta; Sakakibara, Yogo; Minoshima, Masafumi; Sugiyama, Hiroshi

CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa-Oiwakecho, Sakyo, Kyoto, 606-8502, Japan

SOURCE: Cancer Science (2006), 97(3), 219-225
CODEN: CSACCM; ISSN: 1347-9032

PUBLISHER: Blackwell Publishing Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

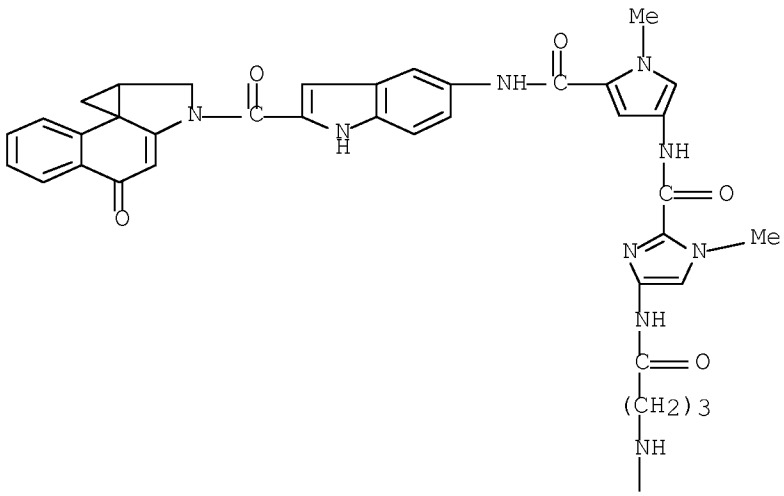
AB DNA-targeting agents, including cisplatin, bleomycin and mitomycin C, are used routinely in cancer treatments. However, these drugs are extremely toxic, attacking normal cells and causing severe side effects. One important question to consider in designing anticancer agents is whether the introduction of sequence selectivity to DNA-targeting agents can improve their efficacy as anticancer agents. In the present study, the growth inhibition activities of an indole-seco 1,2,9,9a- tetrahydrocyclopropa[1,2-c]benz[1,2-e]indol-4-one (CBI) (1) and five conjugates with hairpin pyrrole-imidazole polyamides (2-6), which have different sequence specificities for DNA alkylation, were compared using 10 different cell lines. The av. values of -log GI50 (50% growth inhibition concn.) for compds. 1-6 against the 10 cell lines were 8.33, 8.56, 8.29, 8.04, 8.23 and 8.83, showing that all of these compds. strongly inhibit cell growth. Interestingly, each alkylating agent caused significantly different growth inhibition patterns with each cell line. In particular, the correlation coeffs. between the -log GI50 of compd. 1 and its conjugates 2-6 showed extremely low values (R < 0). These results suggest that differences in the sequence specificity of DNA alkylation lead to marked differences in biol. activity. Comparison of the correlation coeffs. between compds. 6 and 7, with the same sequence specificity as 6, and MS-247, with sequence specificity different from 6, when used against a panel of 37 human cancer cell lines further confirmed the above hypothesis.

IT 865113-64-0 865113-66-2 865113-67-3
885028-77-3 912572-04-4
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of pyrolle-imidazole CBI conjugates with indole linker)

RN 865113-64-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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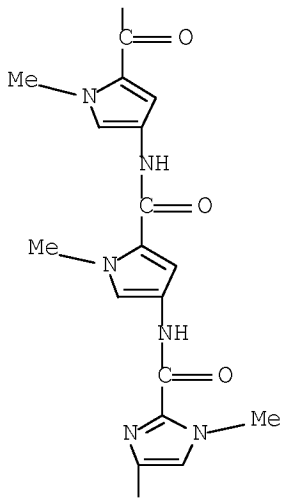

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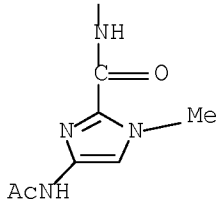

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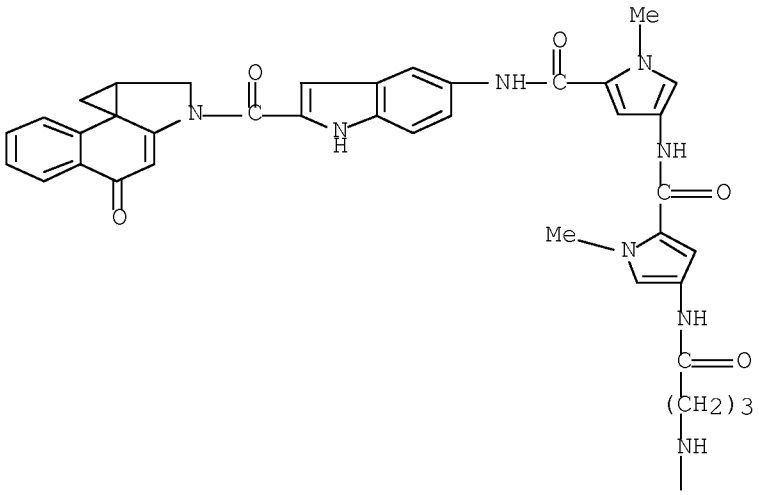

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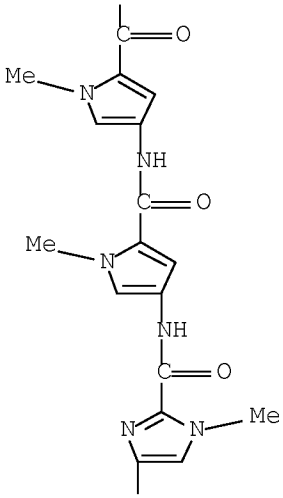

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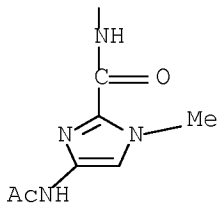

RN 865113-67-3 CAPLUS

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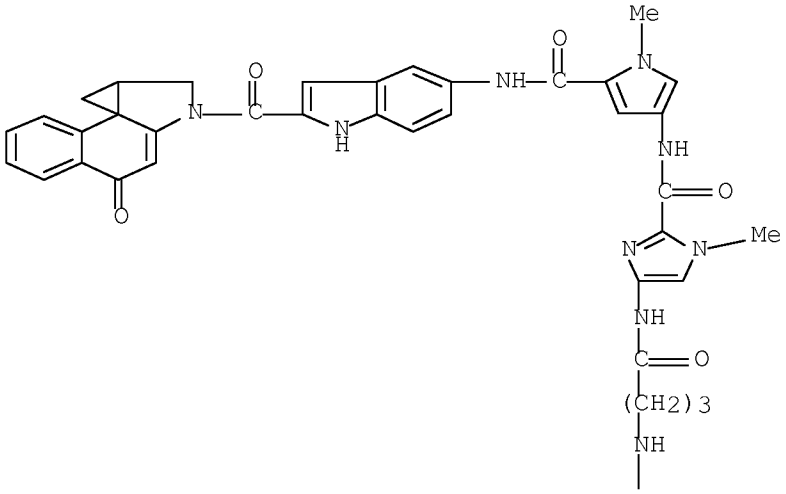

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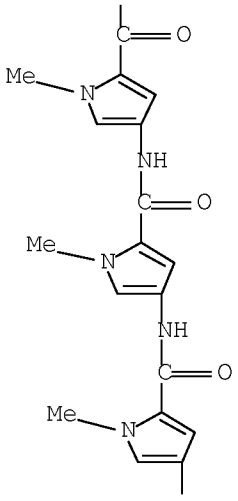

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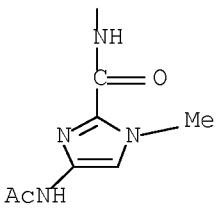

RN 885028-77-3 CAPLUS

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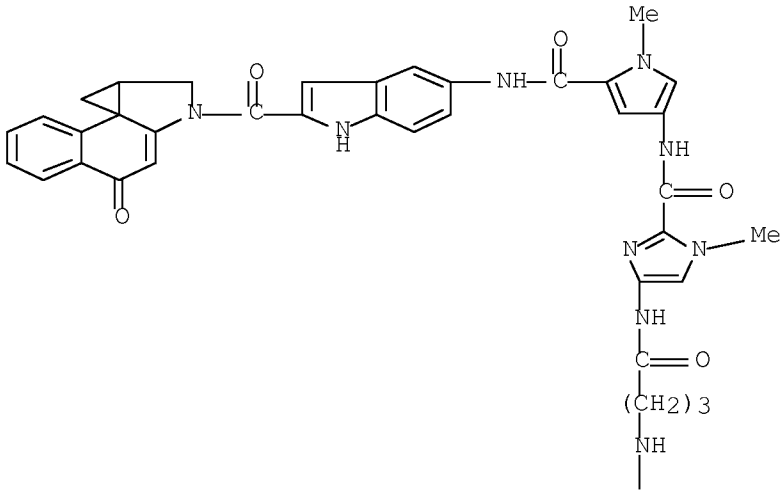
PAGE 1-A



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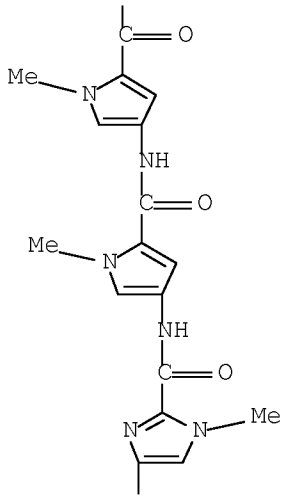

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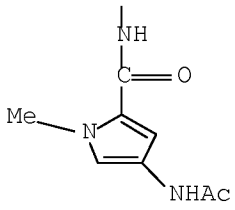

RN 912572-04-4 CAPLUS
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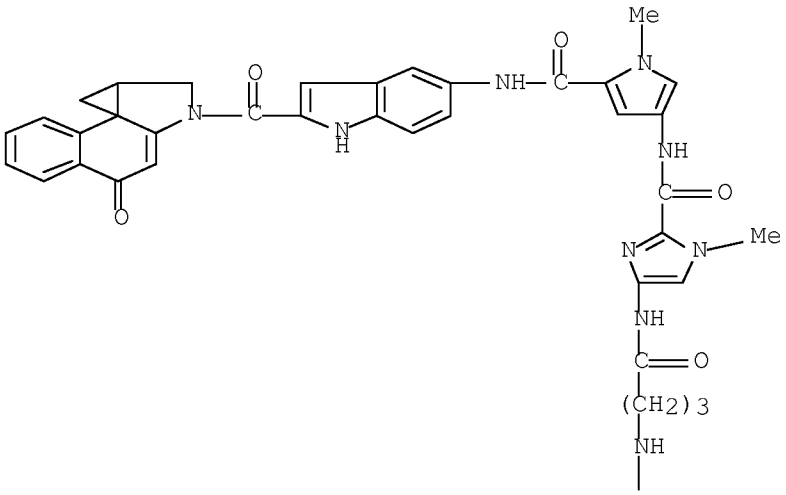

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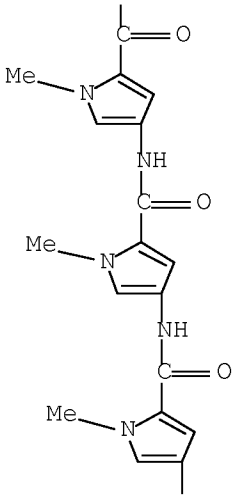

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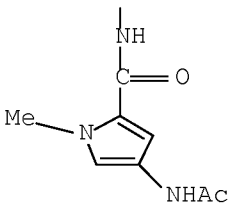

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L11 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:207991 CAPLUS Full-text
DOCUMENT NUMBER: 144:426676
TITLE: Alkylation of template strand of coding region causes effective gene silencing
AUTHOR(S): Shinohara, Ken-ichi; Sasaki, Shunta; Minoshima, Masafumi; Bando, Toshikazu; Sugiyama, Hiroshi
CORPORATE SOURCE: Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa-Oiwakecho, Sakyo, Kyoto, 606-8502, Japan
SOURCE: Nucleic Acids Research (2006), 34(4), 1189-1195
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We recently developed a new type of pyrrole (Py)-imidazole (Im) polyamide-tetrahydrocyclopropabenzindolone (CBI) conjugate with an indole linker as a stable sequence-specific alkylating agent. In this study, we investigated the gene silencing activities of polyamides A, B and C, which selectively alkylate specific sequences in the promoter region, non-coding strand and coding strand, resp., of the green fluorescent protein (GFP) gene. GFP vectors were transfected into human colon carcinoma cells (HCT116), and the cells were treated with 100 nM of the polyamides for 24 h. Fluorescence microscopy indicated that a significant redn. of GFP fluorescence was only obsd. in the cells that were treated with polyamide C. In clear contrast, polyamides A and B did not show such activity. Moreover, real-time PCR demonstrated selective redn. of the expression of GFP mRNA following treatment with polyamide C. These results suggest that alkylating Py-Im polyamides that target the coding strand represent a novel approach for sequence-specific gene silencing.

IT 865113-64-0 865113-67-3 885028-77-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alkylation and gene silencing by; alkylation of template strand of coding region causes effective gene silencing)

RN 865113-64-0 CAPLUS
CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

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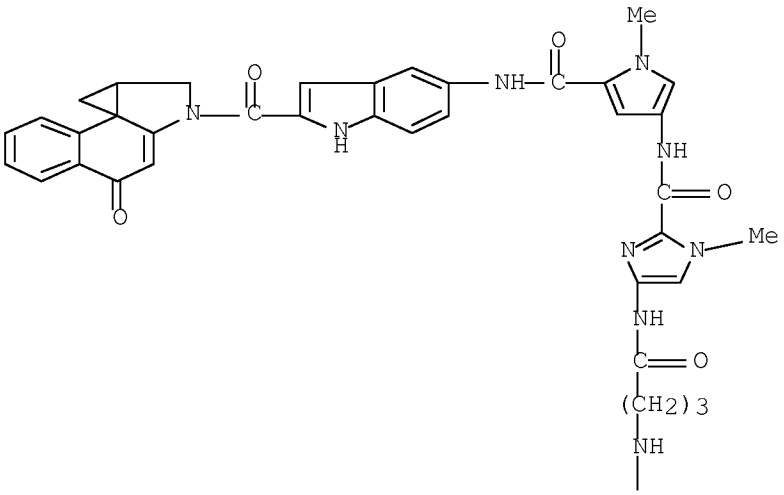

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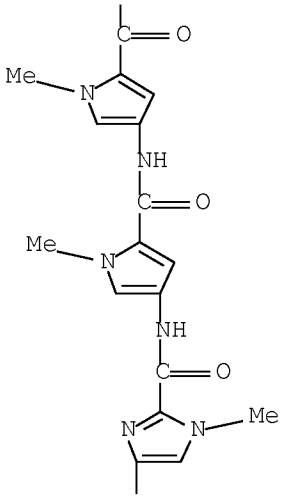

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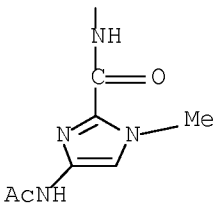
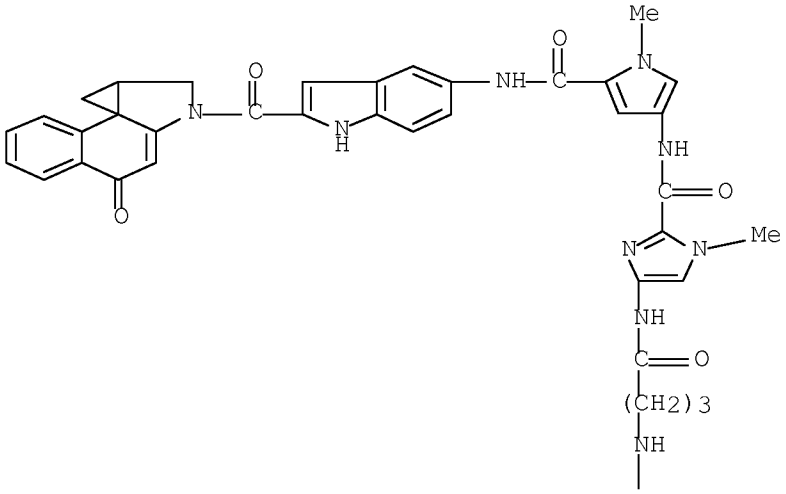


RN 865113-67-3 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-(acetylamino)-N-[5-[[[5-[[[5-[[[4-[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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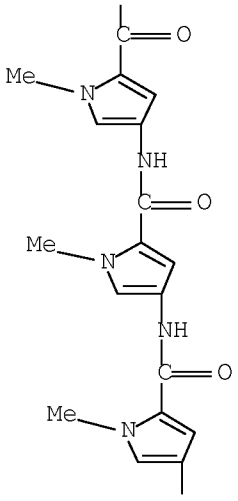

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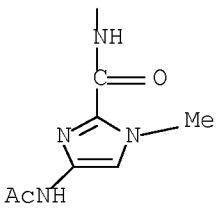

RN 885028-77-3 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

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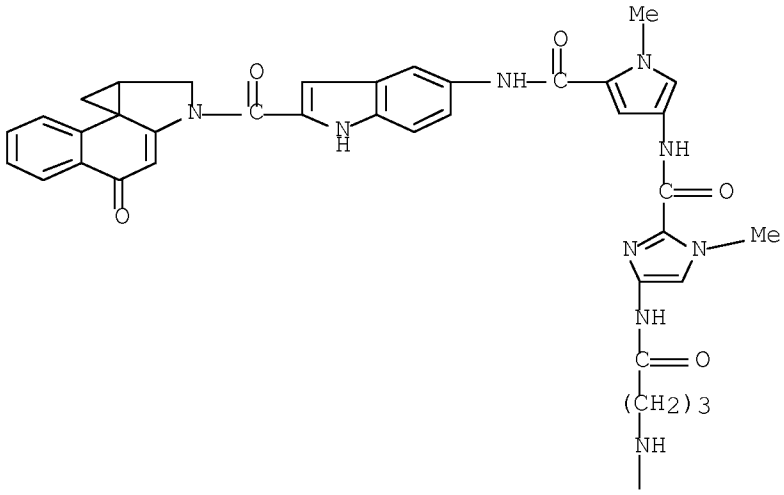

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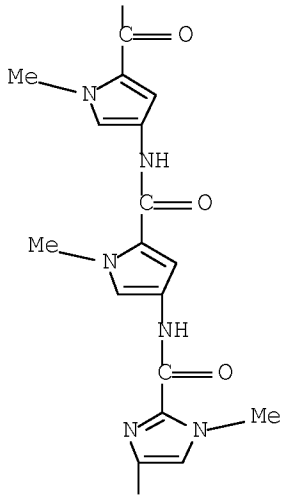

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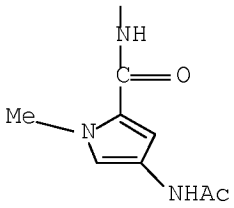

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L11 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1026947 CAPLUS Full-text
DOCUMENT NUMBER: 143:326365
TITLE: Preparation of indole derivatives for alkylating specific base sequence of DNA
INVENTOR(S): Sugiyama, Hiroshi; Bando, Toshikazu
PATENT ASSIGNEE(S): TMRC Co., Ltd., Japan
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087762	A1	20050922	WO 2005-JP4250	20050310

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

				Current application	
	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1731519	A1	20061213	EP 2005-720521		20050310
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US 20070191260	A1	20070816	US 2006-598789		20060912
KR 2007020425	A	20070221	KR 2006-718793		20060913
IN 2006MN01132	A	20070420	IN 2006-MN1132		20060922
PRIORITY APPLN. INFO.:			JP 2004-114793	A	20040313
			WO 2005-JP4250	W	20050310

OTHER SOURCE(S): MARPAT 143:326365
GI

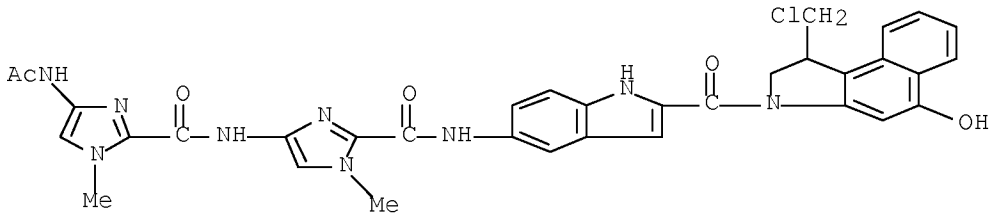
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = functional group alkylating DNA;; R2 = H, alkyl, acyl; X = II, etc.] were prepd. For example, EDCI mediated amidation of compd. III [R = 2-carboxyindol-5-ylamino], e.g., prepd. from III [R = OH] in 2 steps, with 1-(chloromethyl)-2,3-dihydro-1H-benz[e]indol-5-ol followed treatment with aq. NaHCO3 afforded compd. IV. In antitumor activity assays for 39 cancer cell lines (in vitro), the av. IC50 value of compd. IV was 100 nM. Compds. I are claimed useful as DNA alkylating agents.

IT 865113-60-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of indole derivs. as DNA alkylating agents)

RN 865113-60-6 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-(acetylamino)-N-[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)

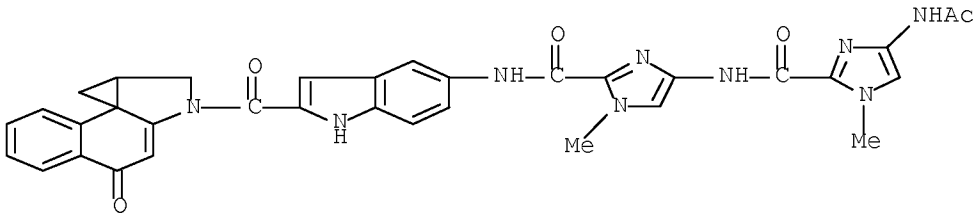


IT 865113-61-7P 865113-64-0P 865113-65-1P
865113-66-2P 865113-67-3P 865113-68-4P
865113-69-5P 865113-70-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole derivs. as DNA alkylating agents)

RN 865113-61-7 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-(acetylamino)-N-[2-[[[2-[(1a,2-dihydro-5-oxo-1H-benzo[e]cycloprop[c]indol-3(5H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-1-methyl- (CA INDEX NAME)



RN 865113-64-0 CAPLUS

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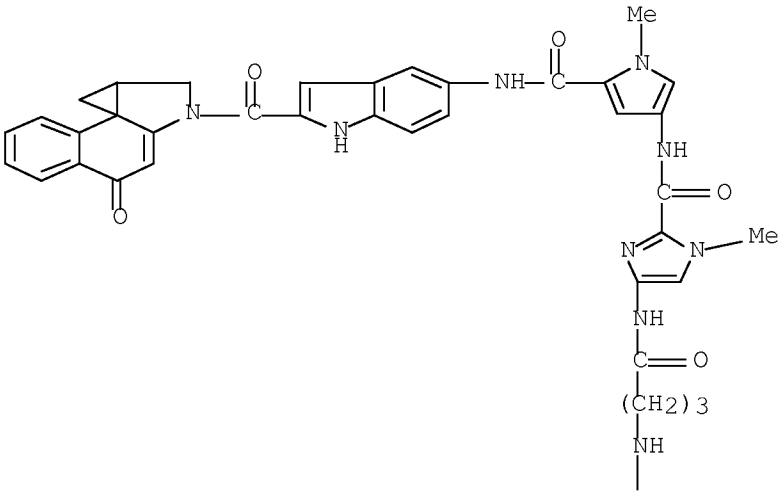
PAGE 1-A



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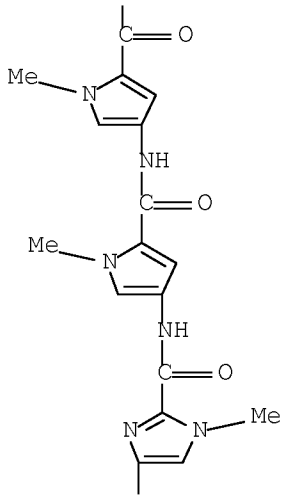

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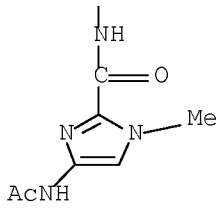

RN 865113-65-1 CAPLUS

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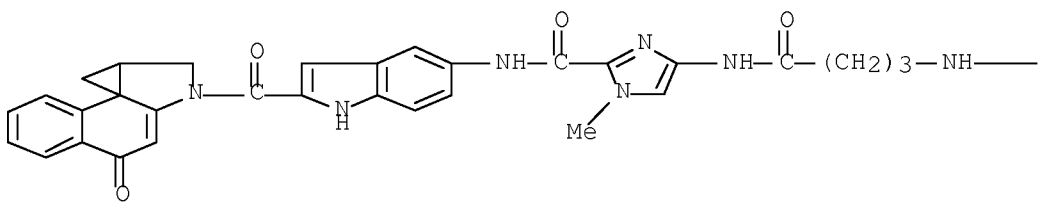
PAGE 1-A



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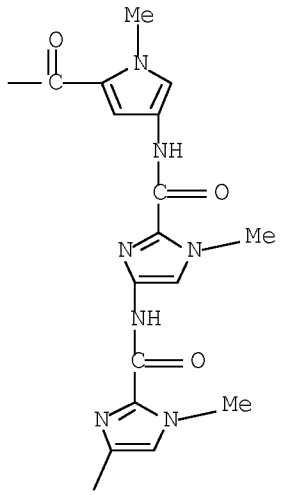

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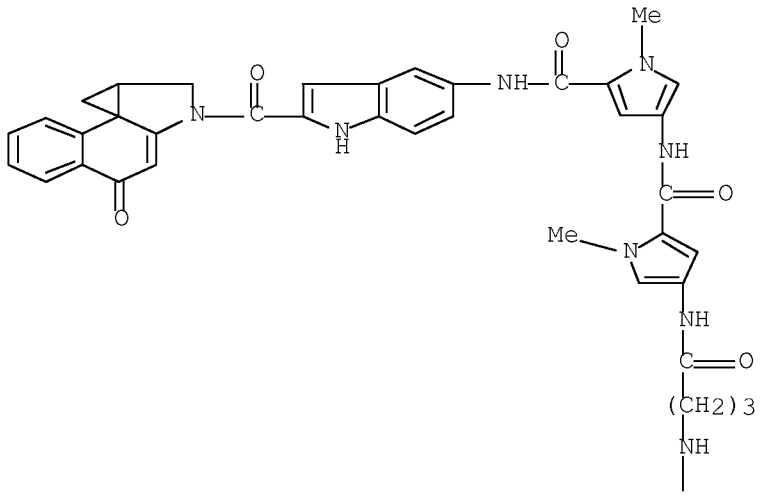
PAGE 1-A



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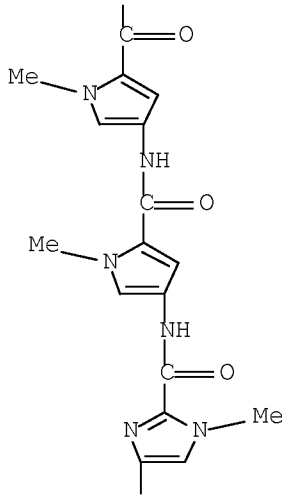

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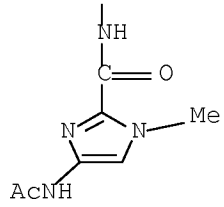

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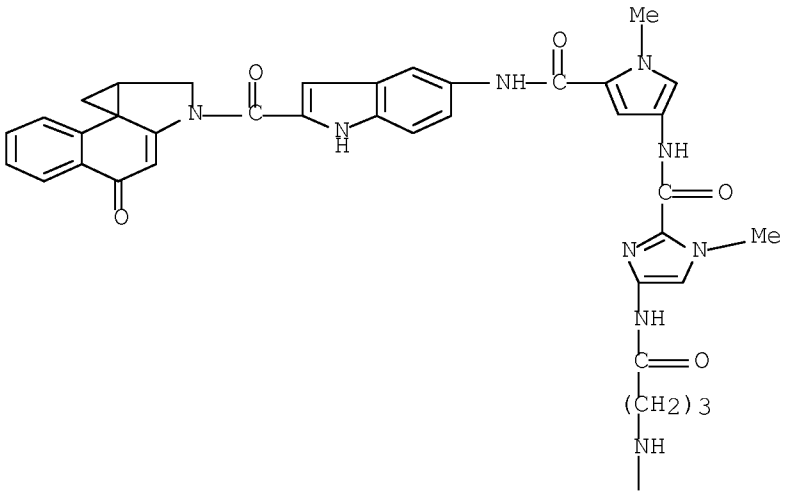

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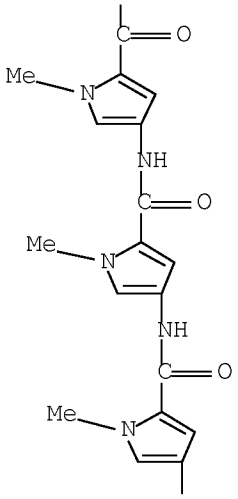

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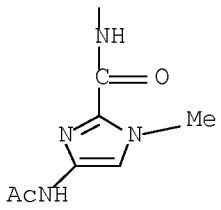

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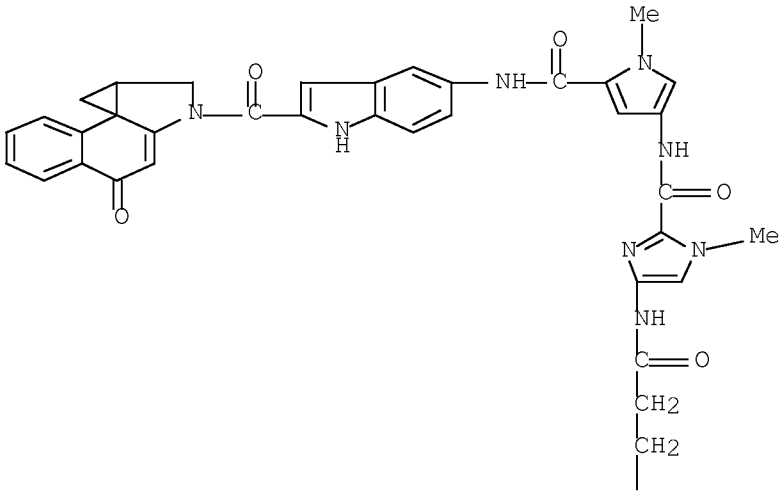
PAGE 1-A



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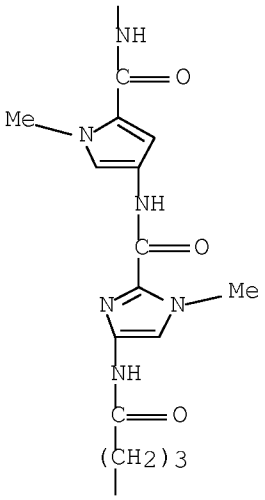

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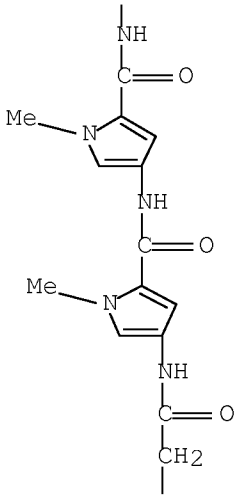

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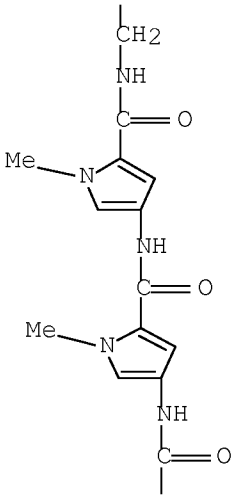

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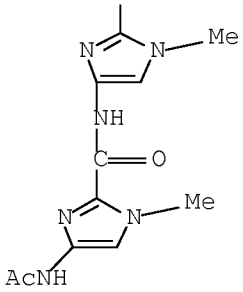
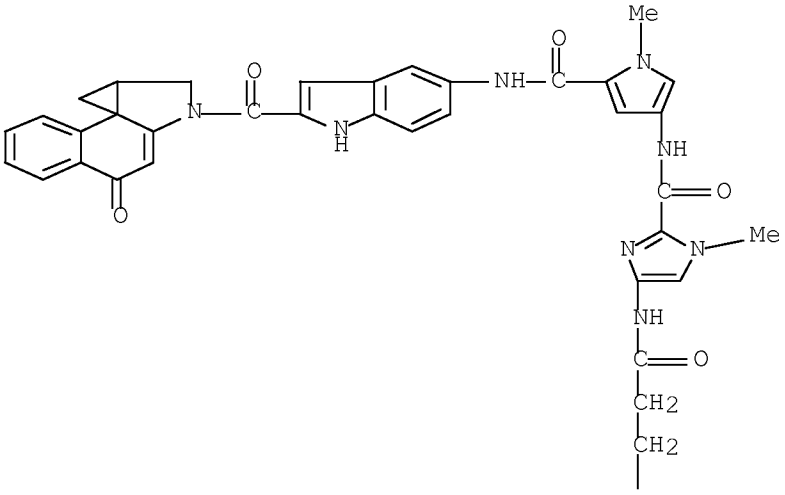


RN 865113-69-5 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[3-[[2-[[[5-[[[2-[(9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl)carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-3-oxopropyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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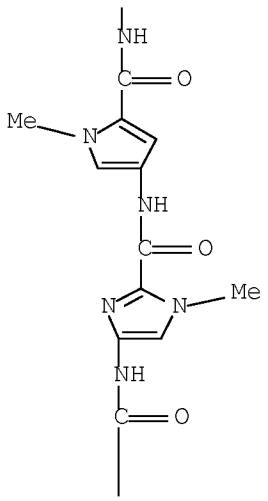

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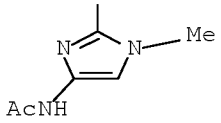

RN 865113-70-8 CAPLUS

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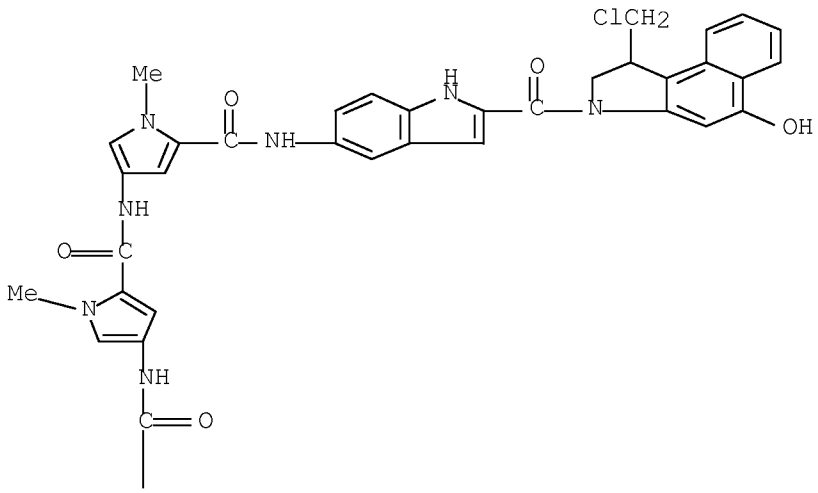

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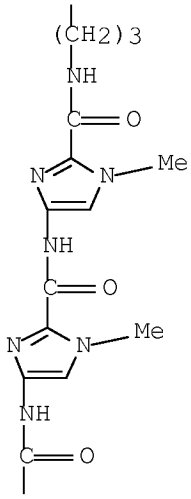

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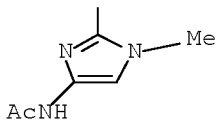
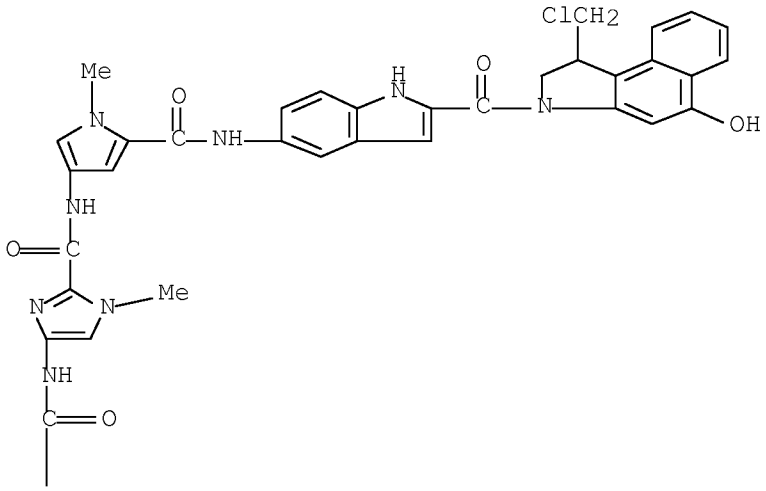


IT 865113-72-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of indole derivs. as DNA alkylating agents)

RN 865113-72-0 CAPLUS

CN 1H-Imidazole-2-carboxamide, 4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-N-[5-[[[5-[[[4-[[2-[[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]-4-oxobutyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl- (CA INDEX NAME)

PAGE 1-A



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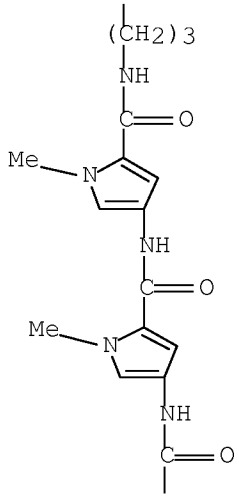
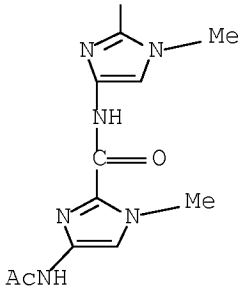




REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:696700 CAPLUS Full-text
DOCUMENT NUMBER: 139:219341
TITLE: DNA-binding amide-drug conjugates
INVENTOR(S): Szekely, Zoltan; Hariprakasha, Humcha Krishnamurthy; Cholody, Marek W.; Michejda, Christopher J.
PATENT ASSIGNEE(S): The Government of the United States of America, Represented by the Secretary Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072058	A2	20030904	WO 2003-US6006	20030227
WO 2003072058	A3	20040805		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003217782	A1	20030909	AU 2003-217782	20030227
US 20050096261	A1	20050505	US 2004-506085	20041001

PRIORITY APPLN. INFO.:

US 2002-361050P	P	20020227
US 2002-370168P	P	20020405
WO 2003-US6006	W	20030227

OTHER SOURCE(S): MARPAT 139:219341

AB An amide conjugate comprising a DNA intercalator binds to the minor groove of DNA. A compn. comprising the conjugate and a carrier is useful for treating cancer in a mammal. Thus, 1-(chloromethyl)-5-hydroxy-1,2-dihydro- 3H-

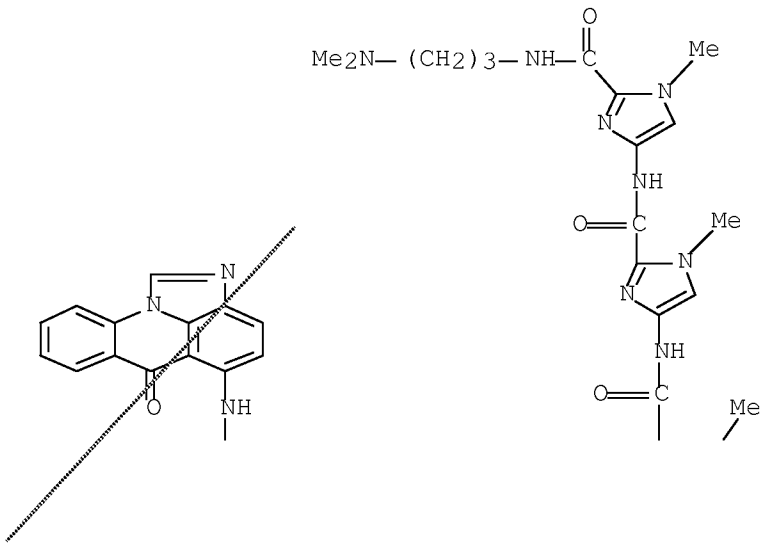
benz[e]indole-8-carboxylic acid (CBIr), a rigid DNA alkylator, was prepd. and conjugated to an imidazole-contg. deriv.

IT 591248-21-4 591248-24-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA-binding polyamide drug conjugates)

RN 591248-21-4 CAPLUS

CN 1H-Benz[e]indole-8-carboxamide, 1-(chloromethyl)-N-[2-[[[2-[[[2-[[[2-[[[3-(dimethylamino)propyl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-2,3-dihydro-5-hydroxy-3-[[5-[[[1-methyl-4-[[1-oxo-3-[[3-[4-[3-[(6-oxo-6H-imidazo[4,5,1-de]acridin-5-yl)amino]propyl]-1-piperazinyl]propyl]amino]propyl]amino]-1H-imidazol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]- (CA INDEX NAME)

PAGE 1-A



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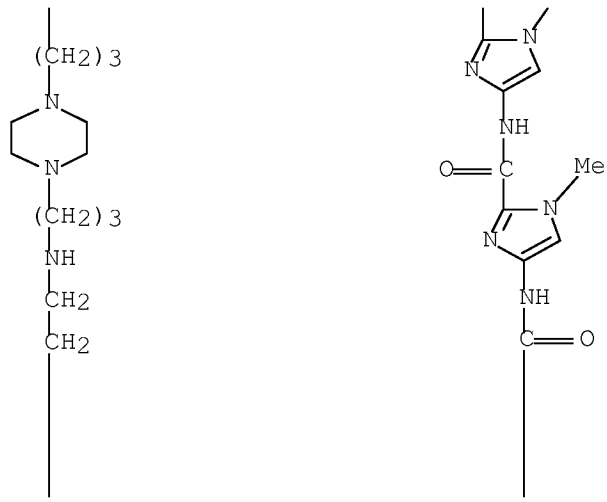

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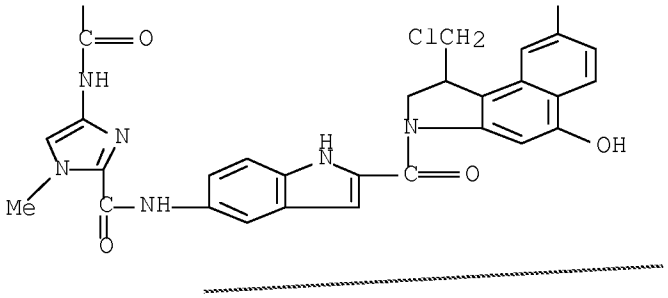
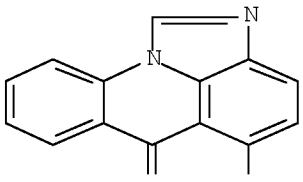
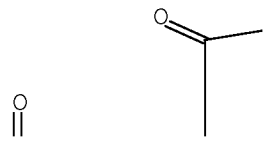


RN 591248-24-7 CAPLUS
CN 5,12-Naphthacenedione, 10-[[3-[[4-[[5-[[[2-[[1-(chloromethyl)-8-[2-[[5-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-[[[1-methyl-5-[[[1-methyl-2-[[[3-[4-[3-[(6-oxo-6H-imidazo[4,5,1-de]acridin-5-yl)amino]propyl]-1-piperazinyl]propyl]amino]carbonyl]-1H-imidazol-4-yl]amino]carbonyl]-1H-pyrrol-3-yl]amino]carbonyl]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-4-hydroxy-1-methyl-1H-pyrrol-3-yl]amino]-2-oxoethyl]-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]-4-oxobutyl]amino]-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





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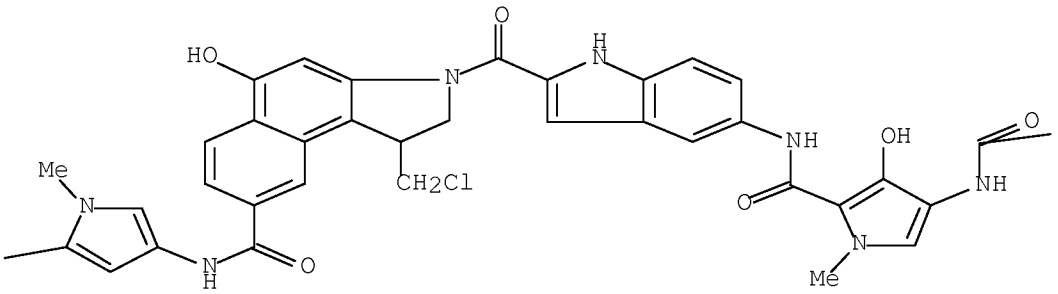

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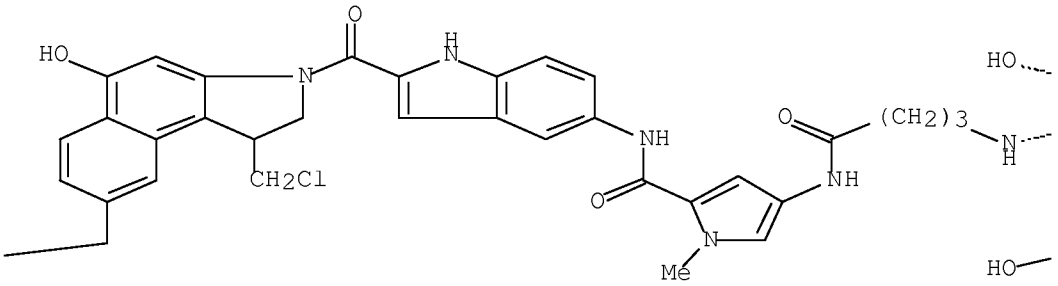

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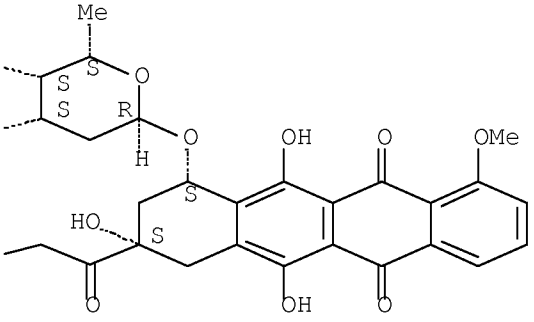

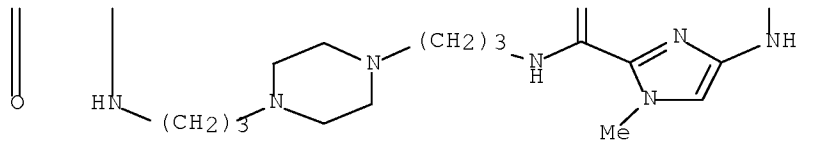

L11 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:221652 CAPLUS Full-text
DOCUMENT NUMBER: 138:255007
TITLE: Preparation of CBI analogues of CC 1065 and the duocarmycins for therapeutic use as anticancer agents
INVENTOR(S): Boger, Dale L.
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022806	A2	20030320	WO 2002-US28749	20020909
WO 2003022806	A3	20031113		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2459308	A1	20030320	CA 2002-2459308	20020909
AU 2002333548	A1	20030324	AU 2002-333548	20020909
EP 1423110	A2	20040602	EP 2002-798201	20020909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005502703	T	20050127	JP 2003-526882	20020909
US 20050014700	A1	20050120	US 2004-489006	20040827
PRIORITY APPLN. INFO.:			US 2001-318179P	P 20010907
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OTHER SOURCE(S): MARPAT 138:255007
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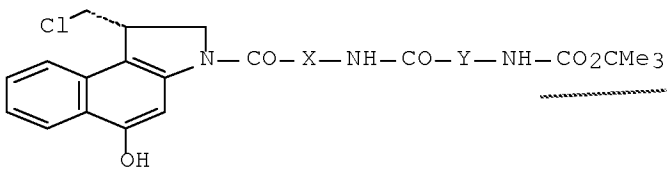


I

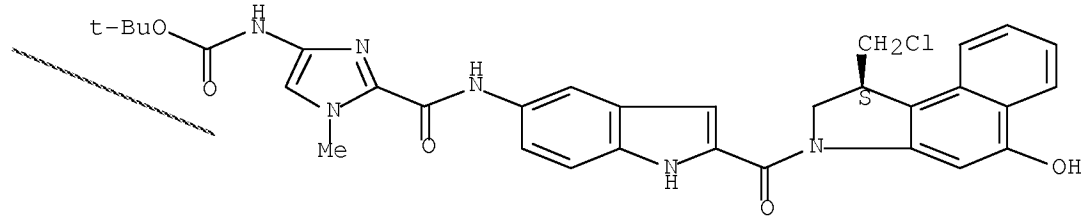
AB 132 CBI analogs I [X, Y = arylene, heteroarylene] of CC 1065 and the duocarmycins having dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents were synthesized by a parallel route. The resultant analogs were evaluated with respect to their catalytic and cytotoxic activities. The relative contribution of the various dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents within the DNA binding domain were characterized. Several of the resultant CBI analogs of CC 1065 and the duocarmycins were characterized as having enhanced catalytic and cytotoxic activities and were identified as having utility as anti-cancer agents. Thus, I (X = Y = -4-C6H4-) was prepd. starting from 4-H2NC6H4CO2H and the hydrochloride salt of seco-CBI.

IT 372954-19-3P 372954-20-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RN 372954-19-3 CAPLUS
CN Carbamic acid, [2-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

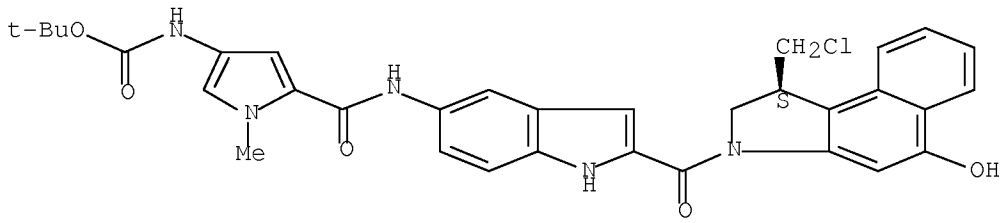
Absolute stereochemistry.

acyl vs.



RN 372954-20-6 CAPLUS
CN Carbamic acid, [5-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



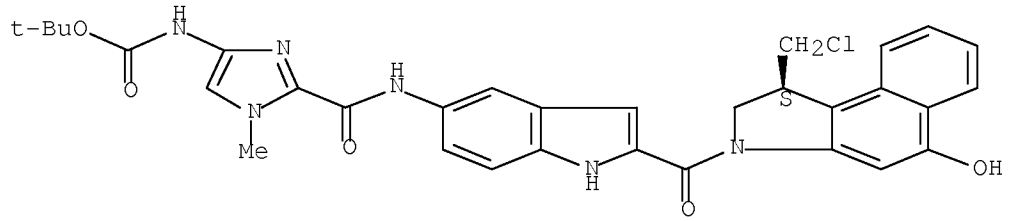
L11 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:667407 CAPLUS Full-text
DOCUMENT NUMBER: 135:357786
TITLE: Parallel Synthesis and Evaluation of 132 (+)-1,2,9,9a-Tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) Analogues of CC-1065 and the Duocarmycins Defining the Contribution of the DNA-Binding Domain
AUTHOR(S): Boger, Dale L.; Schmitt, Harald W.; Fink, Brian E.; Hedrick, Michael P.
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Organic Chemistry (2001), 66(20), 6654-6661
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:357786

AB The soln.-phase, parallel synthesis and evaluation of a library of 132 (+)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) analogs of CC-1065 and the duocarmycins contg. dimeric monocyclic, bicyclic, and tricyclic heteroarom. replacements for the DNA-binding domain are described. This systematic study revealed clear trends in the structural requirements for observation of potent cytotoxic activity and DNA alkylation efficiency, the range of which spans a magnitude of .gtoreq.10 000-fold. Combined with related studies, these results highlight that the role of the DNA-binding domain goes beyond simply providing DNA-binding selectivity and affinity (10-100-fold enhancement in properties), consistent with the proposal that it contributes significantly to catalysis of the DNA alkylation reaction accounting for as much as an addnl. 1000-fold enhancement in properties.

IT 372954-19-3P 372954-20-6P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

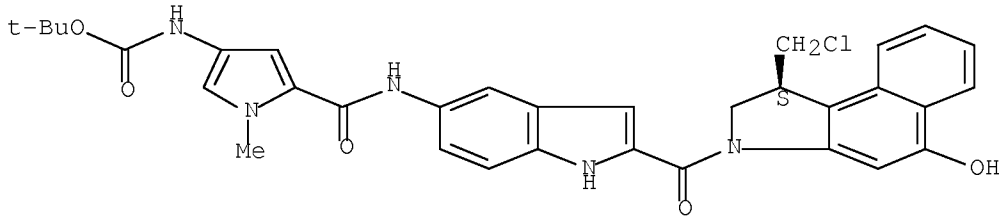
RN 372954-19-3 CAPLUS
CN Carbamic acid, [2-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-imidazol-4-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 372954-20-6 CAPLUS
CN Carbamic acid, [5-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	92.96	520.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.80	-20.00

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 21:44:28 ON 08 JUL 2008